Interleukin (IL)-1 Inhibitors Prior Authorization with Quantity Limit Program Summary

This program applies to MN Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date 03-15-2024

Date of Origin 02-01-2019

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Arcalyst® (rilonacept) Subcutaneous injection	Treatment of Cryopyrin Associated Periodic Syndrome (CAPS), including Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 years and older Maintenance of remission of deficiency of interleukin-1 receptor antagonist (DIRA) in adults and pediatric patients weighing at least 10 kg Treatment of recurrent pericarditis (RP) and reduction in risk of recurrence in adults and pediatric patients 12 years and older		1

Ilaris®
 	
(canakinumab)
 	
Subcutaneous injection
	Periodic Fever Syndromes:
	• Treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) in adults and children 4 years of age and older including:
	  ○ Familial Cold Auto-inflammatory Syndrome (FCAS) and
	  ○ Muckle-Wells Syndrome (MWS)
	• Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) in adult and pediatric patients
	• Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adult and pediatric patients
	• Familial Mediterranean Fever (FMF) in adult and pediatric patients
	• Active Still's disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA) in patients aged 2 years and older
	
	Gout flares in adults in whom non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine are contraindicated, are not tolerated, or do not provide adequate response, and in whom repeated courses of corticosteroids are not appropriate
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See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Cryopyrin-Associated Periodic Syndromes (CAPS)	Cryopyrin-associated periodic syndrome (CAPS) is a rare autosomal dominant hereditary autoimmune disorder associated with a defect in the cryopyrin protein.(2). CAPS syndrome is caused by a gain of function mutation in the NLRP3 gene leading to over secretion of fever causing cytokine IL-1B.(13) There are three distinct

	phenotypes related to a defect in the same gene but differ in the organs involved. The CAPS spectrum includes mild, moderate, and disease severity.(2) Familialsevere phenotypes. The mild phenotype is called familial cold autoinflammatory syndrome (FCAS) is the mildest form and more common in the United States.), the moderate phenotype is also known as Muckle-Wells syndrome (MWS) is the intermediate phenotype and more common in Europe. Neonatal), the neonatal-onset multisystem inflammatory disease (NOMID))/chronic infantile neurologic cutaneous articular syndrome (CINCA) describes the severe phenotype. CAPS is the least common disease and is the most severe form.(6) An international task force recommends bothdiagnosed clinically and genetically. There are more than 240 sequence variants of the followingNLRP3 gene and mutations in this gene are not inclusive of a CAPS diagnosis. The diagnostic criteria need to be present for of CAPS recognize that all but a diagnosis of CAPS few patients with CAPS have detectable systemic inflammation and use unique CPS-specific clinical features along the whole disease spectrum to achieve reasonable specificity and its subtypessensitivity to aid clinicians in making the CAPS diagnosis. These diagnostic criteria do not include genetic confirmation, and therefore can be applied in places where genetic testing is not available. The diagnostic criteria for CAPS are as follows:(13)
	
	• Raised inflammatory markers (CRP/SAA)
	• The presence of at least two of the following signs/symptoms:
	  ○ Urticaria-like rash
	  ○ Cold/stress triggered episodes
	  ○ Sensorineural hearing loss
	  ○ Musculoskeletal symptoms of arthralgia/arthritis/myalgia
	  ○ Chronic aseptic meningitis
	  ○ Skeletal abnormalities of epiphyseal overgrowth/frontal bossing
	
	FCAS is characterized by a hive-likeepisodes of rash that is associated with, fever. and joint pain following generalized exposure to cold and other environmental triggers. Attacks usually occur 1-2 hours after exposure and with symptoms lasting up tolast less than 24 hours.(2) Patients experience urticaria, arthralgia, fever with chills, severe thirst, red-eyes, and headache after a general cold exposure, including air conditioning. In MWS, inflammation can occur spontaneously as well as from triggers, such as stress, cold, or exercise, with episodes lasting from one to three days. MWS shares the same characteristics as FCAS, but is also characterized by renal amyloidosis, sensorineural hearing loss, and conjunctivitis. Hearing loss, partial or complete, often develop by teenage years.(6)
	
	NOMID is characterized by neonatal onset of cutaneous symptoms along with fever with inflammation in multiple organ systems. NOMID shares most of the same characteristics with FCAS and MWS, but also has more severe arthropathy, chronic urticaria, and CNS involvement. CNS manifestations range from hearing loss to aseptic meningitis and mental disabilities. Arthropathy typically affects the large joints, resulting in joint enlargement and functional disability.(6)
	
	Interleukin (IL)-1- beta inhibitors (anakinra, rilonacept, and canakinumab) have shown effectiveness in preventing and alleviating symptoms of CAPS and reducing levels of inflammatory indices, including serum amyloid A.(2) Treatment with non-steroidal anti-inflammatory drugs, disease modifying antirheumatic drugs, and glucocorticoids were offered only some patients partial symptom control.(6) NOMID is a rare chronic inflammatory disease. NOMID is characterized by fever, urticarial rash, aseptic meningitis, deforming arthropathy, hearing loss, and intellectual disability. An urticaria-like rash develops within the first six weeks of life, and a characteristic bony overgrowth predominantly involving the knees develops in most affected children. Therapies are aimed at suppressing inflammation and have included high-dose corticosteroids, disease-modifying antirheumatic drugs, and biologic agent targeting tumor necrosis factor (TNF). Selective blockade of interleukin-1B is effective in the pathophysiology and organ-specific manifestations of NMOSD, in particular the CNS manifestations of the disease.(5)

	Treatment aims are to suppress systemic inflammation, to improve functionality, to prevent organ damage, and to increase patients' quality of life. To achieve these aims, cytokine targeting drugs are important and evidence-based treatment. Since IL-1 plays a central role in CAPS pathogenesis, the anti-IL1 treatments (anakinra, canakinumab, and rilonacept) are recommended for the whole CAPS spectrum.(13)
Deficiency of the IL-1 Receptor Antagonist (DIRA)	Systemic autoinflammatory diseases (SAIDs) are a group of multisystem immunodysregulatory disorders caused primarily by the dysfunction of the innate immune system. Currently, SAIDs are comprised of a wide range of disorders with systemic and organ-specific inflammation in the absence of infections or autoimmunity. In a subset of genetically defined SAIDs, the pathogenesis is driven by increased release or signaling of the pro-inflammatory cytokine IL-1.(7) Patients with DIRA present with early-onset pustular rashes that can be triggered by mechanical stress (pathergy), with sterile osteomyelitis, and nail changes (onychomadesis). Although inflammatory markers are typically highly elevated, fever may be absent. Vertebral involvement can include odontoid osteomyelitis resulting in destruction and neck instability, vertebral block formation and gibbus-like spinal changes that need to be screened for by MRI or CT. The differential diagnosis for DIRA includes chronic recurrent multifocal osteomyelitis (CRMO), synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome and pustular psoriasis. Genetic testing for monogenic defects with overlapping clinical features should include LPIN2, FGR, FBLIM1 for CRMO, CARD14 for CARD14-Mediated Psoriasis (CAMPS), IL36RN for Deficiency of IL-36 Receptor Antagonist (DITRA), AP1S3 for other pustular psoriasis and MEFV for Pyrin-Associated Autoinflammation with Neutrophilic Dermatosis (PAAND).(7) Aims of therapy are early control of disease activity, prevention of disease and treatment related damage, and optimal health-related quality of life. The ultimate goal of a treat-to-target approach is complete remission. In absence of a consensus definition of remission or minimal disease activity for these diseases, remission has been defined for clinical studies and clinical monitoring as an absence of clinical symptoms and normal inflammatory markers. Anakinra and rilonacept both block IL-1α and IL-1β and should be used for DIRA patients.(7)
Recurrent Pericarditis	Pericarditis is inflammation of the pericardial layers around the heart and is the most common form of pericardial disease. Pericarditis may be caused infections, post-cardiac injury syndrome, or pericarditis may be idiopathic. Pericarditis is categorized into four types, acute, incessant, recurrent, and chronic. These categories are based on the length of time of the attack and the presentation. Acute pericarditis is an event lasting 4 weeks or less, incessant is an event lasting more than 4 weeks without a remission, recurrent pericarditis is new signs and symptoms of pericarditis after a symptom-free interval of 4 to 6 weeks, and chronic is an event lasting more than 3 months. Roughly 20% to 30% of patients that develop acute pericarditis will have recurrences, and 50% of patients that have a recurrence will experience more recurrences.(9) The treatment algorithm for therapeutic management of patients with recurrent pericarditis is as follows:(10) • First line therapy: Aspirin or other nonsteroidal anti-inflammatory drug (NSAID) for 1-2 weeks plus colchicine for 6-12 months and exercise restrictions • Second line therapy: Low dose corticosteroids for 1 week plus colchicine • Third line: Aspirin or other NSAID plus colchicine plus corticosteroids triple therapy • Fourth line: IL-1 inhibitors (anakinra, rilonacept) for inflammatory phenotype and azathioprine, IVIG for non-inflammatory phenotype • Fifth line: Pericardiectomy The American College of Cardiology note that mycophenolate mofetil and methotrexate have also been shown to be effective in the treatment of recurrent

	pericarditis that are not responsive to corticosteroids, corticosteroid dependent, or intolerant to corticosteroids.(9)
Periodic Fever Syndromes	Periodic fever syndromes include cryopyrin-associated periodic syndromes (CAPS), familial Mediterranean Fever (FMF), hyperimmunoglobulin D syndrome (HIDS), and tumor necrosis factor (TNF) receptor-1 associated periodic syndrome (TRAPS).(11)
Familial Mediterranean Fever (FMF)	Familial Mediterranean Fever (FMF) is primarily an autosomal recessive disease but there are some reports of the possible autosomal dominant pattern of transmission. FMF manifests as recurrent attacks of fevers with serositis leading to severe chest, abdominal, or joint pain. Episodic attacks typically last 12 to 72 hours. Children with severe disease can have such frequent episodes they do not fully recover and do not grow properly. The most severe complication is the development of secondary amyloidosis with eventual renal failure in uncontrolled patients. FMF results from a mutation in the MEFV gene, which creates the protein pyrin. Pyrin plays a role in the control of the inflammatory system. Mutations lead to uncontrolled inflammation, often triggered by infection, trauma, exercise, menstrual cycles, and psychological stress. Genetic testing may be useful to diagnose patients with FMF, but it is possible for patients to have FMF without a detectable mutation. Roughly 30% of patients in the United States do not have mutations in both genes, making diagnosing FMF difficult.(20) The American College of Rheumatology notes that the diagnosis is generally based on symptoms and physical exam.(7) Colchicine has been the treatment of choice for FMF for decades. The aim of treatment is to prevent attacks, normalize inflammation between the attacks, and prevent the development of amyloidosis. It can also halt the progression of amyloidosis. Colchicine works by inhibiting neutrophil chemotaxis, which is necessary for the inflammatory events in FMF.(20) Colchicine-resistant FMF is defined as frequent attacks despite the maximal tolerable dose of colchicine. Further consensus recommendations have defined it as the occurrence of one or more attacks each month despite receiving the maximally tolerated dose for at least 6 months. Approximately 10% of FMF patients are non-responders to colchicine or do not tolerate it. Interleukin-1 inhibitions is the preferred second line therapy for these patients.(20)
Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)	Hyperimmunoglobulin D Syndrome (HIDS), now known as Mevalonate Kinase Deficiency (MKD), is a genetic syndrome that results in episodes of high fever with skin rash, swollen lymph nodes in the neck, mouth sores, abdominal pain, vomiting, diarrhea, and joint pain with swelling. Fevers tend to be the main symptom lasting 3 to 7 days and recur anywhere from 2 to 12 weeks. MKD is an autosomal recessive disease and results from an abnormality in the mevalonate kinase protein, leading to an increase in the amount of immunoglobulin (especially D). MKD typically develops in early childhood and tends to ease over time. Attacks may be precipitated by vaccination, viral infection, trauma, and stress. Diagnosis may involve checking for inflammatory markers during an attack. Patients with suspected HIDS/MKD should have serum immunoglobulin D and/or immunoglobulin A measured. If elevated IgD with or without elevated IgA may be sufficient to confirm the diagnosis of HIDS/MKD.(3) Patients with normal levels of IgD will require the diagnosis to be confirmed via genetic testing for mutations in the mevalonate kinase gene.(3,8) NSAIDs are recommended first-line therapy for symptomatic treatment of fever and pain associated with HIDS episodes with a duration of 4-7 days, based on the child's pattern. There is no role for NSAID therapy between episodes. Glucocorticoids are the recommended second line treatment option for patients who fail treatment with NSAIDs. Treatment with a biologic agent for prophylaxis and symptomatic treatment is reserved for patients who fail both NSAIDs and glucocorticoids, and prefer treatment over observation due to frequent attacks, severe attacks, or attacks that have a significant impact on quality of life.(3,8)
TNF Receptor-1 Associated Periodic Syndrome (TRAPS)	Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), formerly known as familial Hibernian fever or familial periodic fever, is a rare genetic disease that causes recurrent episodes of fever that last more than a week and are associated with severe muscle pain in the torso and arms. Other symptoms include red and swollen eyes, a red and painful rash, and abdominal pain with nausea, vomiting, and

	diarrhea. TRAPS develops as a result from a defect in the *TNFR1* gene, that encodes the 55 kDa receptor for tumor necrosis factor, leading to an increase in a patient's normal inflammatory response. Persistent, uncontrolled inflammation may lead to the development of amyloidosis. The diagnosis of TRAPS is confirmed via genetic testing for mutations in the *TNFR1* gene.(10,11) NSAIDs may help to control fever, but glucocorticoids are typically required to terminate other clinical features of an attack. Initial dose of 1 mg/kg of prednisone or prednisolone at the start of onset of an attach, followed by a gradual taper and discontinuation after 7-10 days is recommended. Patients with ongoing inflammation from frequent and/or severe attacks are at increased risk of developing amyloidosis. Efficacy data favors the use of IL-1 blockade over anti-TNF therapy in TRAPS, even though there are no head-to-head studies. IL-1 antagonists are the preferred first-line biologic treatment for TRAPS.(13)

Systemic Juvenile Idiopathic Arthritis (SJIA)	Systemic juvenile idiopathic arthritis (SJIA) is a subset of JIA. SJIA is distinct from all other categories of JIA due to fever, rash, and visceral involvement. Disease pathogenesis and cytokine involvement in SJIA are different than other JIA categories. Up to 40% of cases of SJIA are associated with macrophage activation syndrome (MAS), a secondary hemophagocytic syndrome that is a life-threatening complication requiring urgent recognition and treatment. MAS presents with fevers, high ferritin levels, cytopenias, elevated liver enzyme levels, low fibrinogen levels, and high triglyceride levels. As it may occur at any point during the disease course careful monitoring is necessary for children with or without MAS at presentation. Goals of therapy for SJIA includes control of active inflammation and symptoms, and the prevention of a number of disease and/or treatment related morbidities, such as growth disturbances, joint damage, and functional limitations.(21)
	
	SJIA is defined as:(21)
	
	• Patient age 6 months to 18 years
	• Fever of at least 2 weeks duration (daily fever is not required but at some point exhibit a quotidian (daily) fever pattern, defined as a fever that rises to greater than or equal to 39 degrees Celsius at least once a day and returns to less than or equal to 37 degrees Celsius between fever peaks
	• Arthritis in greater than or equal to 1 joint
	• Accompanied by one or more of the following:
	  ○ Evanescent erythematous rash
	  ○ Generalized lymphadenopathy
	  ○ Hepatomegaly or splenomegaly
	  ○ Pericarditis, pleuritis and/or peritonitis
	
	SJIA without MAS
	
	The American College of Rheumatology conditionally recommends IL-1 or IL-6 inhibitors and/or a brief trial of scheduled non-steroidal anti-inflammatories (NSAIDs) for initial treatment for SJIA without MAS. Studies suggest that a small proportion of patients with systemic JIA will respond to NSAIDs alone. If clinical response is not rapid and complete, rapid escalation of therapy is recommended. There is no consensus on the appropriate duration of initial use of NSAIDs before escalating therapy, as many prescribers prefer that the use of NSAIDs be avoided altogether for SJIA. Oral glucocorticoids are conditionally recommended against use in this population (the recommendation is conditional, as IL-1 or IL-6 inhibitors may not always be immediately available, and glucocorticoids may help control systemic and joint manifestations until IL-1 or IL-6 inhibitors can be started. Conventional synthetic disease modifying antirheumatic drugs (DMARDs) are strongly recommended against as initial therapy in this population. For subsequent therapy IL-1 and IL-6 inhibitors are strongly recommended over a single or combination of conventional synthetic DMARDs for inadequate response to intolerance of NSAIDs and/or glucocorticoids.(21)
	
	SJIA with MAS

	The American College of Rheumatology conditionally recommends IL-1 or IL-6 inhibitors over calcineurin inhibitors alone to achieve inactive disease and resolution of MAS. Glucocorticoids are conditionally recommended as part of initial treatment in patients with SJIA with MAS. Systemic glucocorticoids may be necessary for severely ill patients because they can have rapid onset of action. Longer-term glucocorticoids therapy in children is not appropriate because of its effects on bone health and growth.(21)
Adult-Onset Still's Disease	Adult-onset Still's disease (AOSD) is a rare systemic, autoinflammatory disorder characterized by arthritis, spiking fever, evanescent rash, and elevated ferritin levels. The underlying cause of AOSD is not fully understood as it is still unknown what exactly triggers damage-associated molecular patterns molecules (DAMPs) and pathogen-associated molecular patterns (PAMPs) to be released from injured tissues. PAMPs and DAMPs stimulate macrophages and neutrophils, leading to activation of specific inflammasomes via Toll-like receptors. Inflammasomes are multiprotein units that act as catalysts by activating the caspase pathway immediately after they come into contact with damage or illness. Caspase enzymes lead to overproduction of IL-1B, the hallmark of AOSD, and IL-18. IL-1B and IL-18 then promote further abnormal inflammation by several cytokine bursts, including IL-6, IL-8, IL-17, IL-18, anti-tumor necrosis factor (TNF) alfa.(19) The hallmark symptoms of AOSD are fever of unknown origin, joint pain, and a maculopapular evanescent rash. Other symptoms can include sore throat, myalgia, enlarged lymph nodes, splenomegaly, hepatomegaly, pleurisy, pericarditis, weight loss, and abdominal pain. Lab tests typically show levels corresponding with the non-specific inflammatory nature of AOSD. Increases in the following lab levels are commonly seen in AOSD: erythrocyte sedimentation rate (ESR), C reactive protein (CRP), white blood cell counts (greater than or equal to 10,000/mm^3 with greater than or equal to 80% polymorphonuclear cells), serum ferritin (five times the normal value [i.e., 1000 mcg/L] is suggestive of AOSD), and liver enzymes.(19) The course of AOSD can be broken down into three different patterns of disease development and progression: monocyclic, polycyclic (aka intermittent), and chronic progressive. Monocyclic AOSD is generally a self-limiting single episode that fades within months. Polycyclic AOSD is associated with multiple flares separated by periods of remission, with flares becoming less severe with time. Chronic progressive AOSD is persistently active disease that typically involves polyarthritis and is the main pattern associated with lasting disability.(19) The diagnosis of AOSD is one of exclusion based on the presence of the most common clinical features and lab values. Infections, neoplastic and autoimmune diseases should be ruled out before considering a diagnosis of AOSD, as they can mimic the clinical manifestations of AOSD. Corticosteroids and NSAIDs are almost always first line therapy for AOSD even though they have a poor overall response. To achieve satisfactory control of the disease, DMARDs such as methotrexate, cyclosporin, or azathioprine are widely used. TNF alfa blockers should only be used in patients in the end stage of the articular type to inhibit erosion progression. Due to the central functional role of IL-1 in the pathogenesis of autoinflammatory conditions, IL-1 receptor antagonists are the first choice for AOSD, yet patients with mainly articular phenotypes do not always benefit. Other therapies that show efficacy are anti IL-6 and Janus kinase (JAK) inhibitors.(19)
Gout	Gout is the most common form of inflammatory arthritis in the US. While the etiology of gout is well-understood and there are effective and inexpensive medications to treat gout, gaps in quality of care persist.(22) Gout appears to be more prevalent in men (5.9%) vs women (2%) and occurs due to the deposition of monosodium urate (MSU) crystals into tissue within the body which occurs because of high uric acid levels (hyperuricemia). The risk of gout increases with advancing age due to increased uric acid levels. The frequency of gout in individuals above the age of 80 is 30-fold higher than in individuals aged 20-29 years. Obesity and metabolic syndrome can also increase the risk of gout.(23)

	Gout can involve almost any joint in the body, but the most common initial joint involved in 50% of cases is the first metatarsal. Other joints commonly involved include joints of the foot and ankle, knees, wrist, fingers, and elbows. Joints involving the spine can occur but are much rarer. Typically, gout flares occur in one joint and begin abruptly within the hours of the night or early morning. There will be warmth and redness with swelling of the joint and can often appear to look like an infection.(23) Like many forms of inflammatory arthritis, gout can present itself in ways in addition to joint pain. Gout can develop tophi, which are aggregated deposits of MSU in different parts of the body such as elbows, knees, the cartilage around the ears, and other areas. It can also develop as uric acid kidney stones. Individuals with gout can have increased risk of heart disease and kidney disease.(23) The 2020 American College of Rheumatology (ACR) guidelines strongly recommend urate-lowering therapy (ULT) for gout patients with any of the following:(22) • Greater than or equal to 1 subcutaneous tophi • Evidence of radiographic damage (any modality) attributable to gout • Frequent gout flares defined as greater than or equal to 2 annually Initiating ULT is conditionally recommended for patients who have previously experienced greater than one flare but have infrequent flares (less than 2 times per year). Initiating ULT is conditionally recommended against in patients with gout experiencing their first gout flare unless the patient has comorbid moderate-to severe-chronic kidney disease (CKD) (stage greater than or equal to 3), serum urate concentration greater than 9 mg/dl, or urolithiasis in which ULT is conditionally recommended as first-line therapy. For patients with asymptomatic hyperuricemia (serum urate levels greater than 6.8 mg/dl with no prior gout flares or subcutaneous tophi) initiating ULT therapy is conditionally recommended against.(22) Treatment with allopurinol is the preferred first-line agent over all ULTs for all patients including those with moderate-to severe CKD. An alternative to allopurinol is febuxostat. It is also strongly recommended to initiate concomitant anti-inflammatory prophylaxis therapy (e.g., colchicine, NSAIDs, prednisone/prednisolone) over no anti-inflammatory prophylaxis. Prophylactic anti-inflammatory treatment should continue for 3 to 6 months. Pegloticase is strongly recommended against as first-line therapy. (22)
Efficacy - Gout	The efficacy of Ilaris was demonstrated in two 12-week, randomized, double-blind, active-controlled studies in patient with gout flares for whom non-steroidal anti-inflammatory drugs (NSAIDs) and or colchicine were contraindicated, not tolerated, or ineffective, and who had experienced at least three gout flares in the previous year. Each study continued in a 12-week, double blind, active-controlled extensions, followed by an open-label extension. The studies were then combined into an open-label extension up to a maximum of 36 months where all patients were treated with Ilaris upon a new flare.(1) In all of the studies pain intensity of the most affected joint (0-100 mm VAS [visual analog scale]) at 72 hours post-dose was consistently lower for patients treated with Ilaris compared with active comparator.(1) In the subpopulation of patients in the 3 studies unable to use NSAIDs and colchicine, time to new flare over 12 weeks from randomization showed a reduction in the risk of a new flare when treated with Ilaris compared with triamcinolone acetonide. (1)
Safety	Arcalyst does not have any FDA labeled contraindications.(1) Ilaris is contraindicated in patients with a confirmed hypersensitivity to the active substance or to any of its excipients.(11)

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23	American College of Rheumatology. Understanding Gout Symptoms & Treatment. April 27, 2023 Rheumatic Disease.

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Ilaris	canakinumab subcutaneous inj	150 MG/ML	M ; N ; O ; Y	N		
Arcalyst	rilonacept for inj	220 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Arcalyst	rilonacept for inj	220 MG	8	Vials	28	DAYS			
Ilaris	canakinumab subcutaneous inj	150 MG/ML	2	Vials	28	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Arcalyst	rilonacept for inj	220 MG	Medicaid
Ilaris	canakinumab subcutaneous inj	150 MG/ML	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Arcalyst	rilonacept for inj	220 MG	Medicaid
Ilaris	canakinumab subcutaneous inj	150 MG/ML	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
Arcalyst	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** No target agents are eligible for continuation of therapy 1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. BOTH of the following: 1. The patient has ONE of the following indications: A. Cryopyrin Associated Periodic Syndrome (CAPS) **OR** B. Familial Cold Auto-Inflammatory Syndrome (FCAS) **OR** C. Muckle-Wells Syndrome (MWS) **AND** 2. BOTH of the following: A. The patient has elevated pretreatment serum inflammatory markers (C-reactive protein/serum amyloid A) **AND** B. The patient has at least TWO symptoms typical for CAPS (i.e., urticaria-like rash, cold/stress triggered episodes, sensorineural hearing loss, musculoskeletal symptoms of arthralgia/arthritis/myalgia, chronic aseptic meningitis, skeletal abnormalities of epiphyseal overgrowth/frontal bossing) **OR** C. BOTH of the following: 1. The patient has a diagnosis of deficiency of interleukin-1 receptor antagonist **AND** 2. The requested agent is being used for maintenance of remission **OR** D. The patient has a diagnosis of recurrent pericarditis AND ONE of the following 1. BOTH of the following: A. The patient's medication history includes colchicine AND ONE of the following: 1. The patient had an inadequate response to colchicine **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over colchicine **AND** B. ONE of the following: 1. Colchicine was used concomitantly with at least a 1 week trial of a non-steroidal anti-inflammatory drug (NSAID) AND a corticosteroid **OR** 2. The patient's medication history includes at least a 1 week trial of a non-steroidal anti-inflammatory (NSAID) AND a corticosteroid AND ONE of the following: A. The patient had an inadequate response to a non-steroidal anti-inflammatory (NSAID) AND a corticosteroid **OR**

Module	Clinical Criteria for Approval
	B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over a non-steroidal anti-inflammatory (NSAID) AND a corticosteroid **OR** 3. The patient has an intolerance or hypersensitivity to BOTH an NSAID AND a corticosteroid **OR** 4. The patient has an FDA labeled contraindication to ALL NSAIDs AND ALL corticosteroids **OR** 2. The patient has an intolerance or hypersensitivity to colchicine **OR** 3. The patient has an FDA labeled contraindication to colchicine **OR** 4. The patient's medication history includes an oral immunosuppressant (i.e., azathioprine, methotrexate, mycophenolate) AND ONE of the following: A. The patient had an inadequate response to an oral immunosuppressant (i.e., azathioprine, methotrexate, mycophenolate) **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over an oral immunosuppressant **OR** 5. The patient has an intolerance or hypersensitivity to oral immunosuppressants used in the treatment of recurrent pericarditis **OR** 6. The patient has an FDA labeled contraindication to oral immunosuppressants used in the treatment of recurrent pericarditis **OR** 7. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 8. The prescriber has provided documentation that colchicine in combination with NSAIDs, systemic corticosteroids, AND oral immunosuppressants cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** E. The patient has another FDA approved indication for the requested agent **OR** F. The patient has another indication that is supported in compendia for the requested agent **AND** 2. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, pediatrician, cardiologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent

<table>
<tr><th>Module</th><th>Clinical Criteria for Approval</th></tr>
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Compendia Allowed: CMS Approved Compendia

Length of Approval: 12 months

NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

Renewal Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through plan's Prior Authorization process AND
2. The patient has had clinical benefit with the requested agent AND
3. The prescriber is a specialist in area of the patient's diagnosis (e.g., allergist, immunologist, pediatrician, cardiologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis AND
4. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table):
A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) OR
B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following:
1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent AND
2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) AND
5. The patient does NOT have any FDA labeled contraindications to the requested agent

Length of Approval: 12 months

NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.
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<tr><td>Ilaris</td><td>
Initial Evaluation

Target Agent(s) will be approved when ALL of the following are met:

1. ONE of the following:
A. The requested agent is eligible for continuation of therapy AND ONE of the following:

<table>
<tr><th>Agents Eligible for Continuation of Therapy</th></tr>
<tr><td>No target agents are eligible for continuation of therapy</td></tr>
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1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days OR
2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed OR
B. BOTH of the following:
1. The patient has ONE of the following indications:
A. Cryopyrin Associated Periodic Syndrome (CAPS) OR
B. Familial Cold Auto-Inflammatory Syndrome (FCAS) OR
C. Muckle-Wells Syndrome (MWS) AND
2. BOTH of the following:
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</table>

Module	Clinical Criteria for Approval
	A. The patient has elevated pretreatment serum inflammatory markers (C-reactive protein/serum amyloid A) **AND** B. The patient has at least TWO of the following symptoms typical for CAPS (i.e., urticaria-like rash, cold/stress triggered episodes, sensorineural hearing loss, musculoskeletal symptoms of arthralgia/arthritis/myalgia, chronic aseptic meningitis, skeletal abnormalities of epiphyseal overgrowth/frontal bossing) **OR** C. The patient has a diagnosis of Familial Mediterranean Fever (FMF) AND ONE of the following: 1. The patient's medication history includes colchicine AND ONE of the following: A. The patient had an inadequate response to colchicine **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over colchicine **OR** 2. The patient has an intolerance or hypersensitivity to colchicine **OR** 3. The patient has an FDA labeled contraindication to colchicine **OR** 4. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 5. The prescriber has provided documentation that colchicine cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** D. BOTH of the following: 1. The patient has a diagnosis of Hyperimmunoglobulin D Syndrome (HIDS) or Mevalonate Kinase Deficiency (MKD) **AND** 2. The patient's diagnosis was confirmed via genetic testing for mutations in the mevalonate kinase (MVK) gene **OR** E. BOTH of the following: 1. The patient has a diagnosis of Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS) **AND** 2. The patient's diagnosis was confirmed via genetic testing for mutations in the TNFR1 gene **OR** F. The patient has a diagnosis of active systemic juvenile idiopathic arthritis (SJIA) AND ALL of the following: 1. The patient has ongoing fever for at least 2 weeks **AND** 2. The patient has arthritis in greater than or equal to 1 joint **AND** 3. The patient has ONE or more of the following: 1. Evanescent erythematous rash 2. Generalized lymphadenopathy 3. Hepatomegaly or splenomegaly 4. Pericarditis, pleuritis and/or peritonitis **OR** G. The patient has a diagnosis of adult-onset Still's disease (AOSD) and BOTH of the following: A. ONE of the following: 1. The patient's medication history includes ONE corticosteroid or ONE non-steroidal anti-inflammatory drug (NSAID) and ONE of the following: A. The patient had an inadequate response to at least ONE corticosteroid or ONE non-steroidal anti-inflammatory drug (NSAID) **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the

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	use of the requested agent over corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) **OR** B. The patient has an intolerance or hypersensitivity to ONE corticosteroid or ONE non-steroidal anti-inflammatory drug (NSAID) **OR** C. The patient has an FDA labeled contraindication to ALL corticosteroids AND ALL non-steroidal anti-inflammatory drugs (NSAIDs) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that ALL corticosteroids and ALL non-steroidal anti-inflammatory drugs (NSAIDs) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 2. ONE of the following: 1. The patient's medication history includes ONE immunosuppressant used in treatment of AOSD (i.e., methotrexate, cyclosporine, azathioprine) AND ONE of the following: A. The patient had an inadequate response to ONE immunosuppressant used in treatment of AOSD (i.e., methotrexate, cyclosporine, azathioprine) **OR** B. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over immunosuppressants used in treatment of AOSD (i.e., methotrexate, cyclosporine, azathioprine) **OR** B. The patient has an intolerance or hypersensitivity to ONE immunosuppressant used in treatment of AOSD (i.e., methotrexate, cyclosporine, azathioprine) **OR** C. The patient has an FDA labeled contraindication to ALL immunosuppressants used in treatment of AOSD (i.e., methotrexate, cyclosporine, azathioprine) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that immunosuppressants used in treatment of AOSD (i.e., methotrexate, cyclosporine, azathioprine) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **OR** H. The patient has a diagnosis of gout flares AND ALL of the following: 1. The patient has experienced greater than or equal to 3 flares in the past 12 months **AND**

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	2. ONE of the following: A. The patient's medication history includes ONE non-steroidal anti-inflammatory drug (NSAID) AND ONE of the following: 1. The patient had an inadequate response to ONE non-steroidal anti-inflammatory drug (NSAID) **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over non-steroidal anti-inflammatory drugs (NSAIDs) **OR** B. The patient has an intolerance or hypersensitivity to ONE non-steroidal anti-inflammatory drug (NSAID) **OR** C. The patient has an FDA labeled contraindication to ALL non-steroidal anti-inflammatory drugs (NSAIDs) **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on the requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that non-steroidal anti-inflammatory drugs (NSAIDs) cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 3. ONE of the following: A. The patient's medication history includes colchicine AND ONE of the following: 1. The patient had an inadequate response to colchicine **OR** 2. The prescriber has submitted an evidence-based and peer-reviewed clinical practice guideline supporting the use of the requested agent over colchicine **OR** B. The patient has an intolerance or hypersensitivity to colchicine **OR** C. The patient has an FDA labeled contraindication to colchicine **OR** D. The patient is currently being treated with the requested agent as indicated by ALL of the following: 1. A statement by the prescriber that the patient is currently taking the requested agent **AND** 2. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** 3. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** E. The prescriber has provided documentation that colchicine cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** 4. Repeated courses of corticosteroids are not appropriate for the patient **OR** I. The patient has another FDA approved indication for the requested agent **OR** J. The patient has another indication that is supported in compendia for the requested agent **AND** 2. If the patient has an FDA approve indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**

Module	Clinical Criteria for Approval
	B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, pediatrician, rheumatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** CMS Approved Compendia **Length of Approval:** 12 weeks for gout flares; 12 months for all other diagnoses NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through plan's Prior Authorization process **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The prescriber is a specialist in area of the patient's diagnosis (e.g., allergist, immunologist, pediatrician, rheumatologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) **AND** 5. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limit for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND**

Module	Clinical Criteria for Approval
	B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **OR** 3. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) exceeds the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: 12 months

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
Agents NOT to be used Concomitantly Abrilada (adalimumab-afzb) Actemra (tocilizumab) Adalimumab Adbry (tralokinumab-ldrm) Amjevita (adalimumab-atto) Arcalyst (rilonacept) Avsola (infliximab-axxq) Benlysta (belimumab) Bimzelx (bimekizumab-bkzx) Cibinqo (abrocitinib) Cimzia (certolizumab) Cinqair (reslizumab) Cosentyx (secukinumab) Cyltezo (adalimumab-adbm) Dupixent (dupilumab) Enbrel (etanercept) Entyvio (vedolizumab) Fasenra (benralizumab)

Contraindicated as Concomitant Therapy
Hadlima (adalimumab-bwwd)
Hulio (adalimumab-fkjp)
Humira (adalimumab)
Hyrimoz (adalimumab-adaz)
Idacio (adalimumab-aacf)
Ilaris (canakinumab)
Ilumya (tildrakizumab-asmn)
Inflectra (infliximab-dyyb)
Infliximab
Kevzara (sarilumab)
Kineret (anakinra)
Litfulo (ritlecitinib)
Nucala (mepolizumab)
Olumiant (baricitinib)
Omvoh (mirikizumab-mrkz)
Opzelura (ruxolitinib)
Orencia (abatacept)
Otezla (apremilast)
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)
Rinvoq (upadacitinib)
Rituxan (rituximab)
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Siliq (brodalumab)
Simponi (golimumab)

Contraindicated as Concomitant Therapy
Simponi ARIA (golimumab)
Skyrizi (risankizumab-rzaa)
Sotyktu (deucravacitinib)
Stelara (ustekinumab)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tysabri (natalizumab)
Velsipity (etrasimod)
Wezlana (ustekinumab-auub)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib extended release)
Xolair (omalizumab)
Yuflyma (adalimumab-aaty)
Yusimry (adalimumab-aqvh)
Zeposia (ozanimod)
Zymfentra (infliximab-dyyb)