Corporate Medical Policy

Canakinumab (Ilaris®)

File Name:	canakinumab_ilaris
Origination:	10/2020
Last CAP Review:	n/a
Next CAP Review:	2/2021
Last Review:	10/2020

Description of Procedure or Service

Canakinumab (Ilaris®) is an interleukin-1β blocker that is indicated for the treatment of the following autoinflammatory periodic fever syndromes: Cryopyrin-Associated Periodic Syndromes (CAPS) in adults and children ≥ 4 years of age to include Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS), Tumor Necrosis Factor (TNF) Receptor-Associated Periodic Syndrome (TRAPS) in adult and pediatric patients, Hyperimmunoglobulin D (Hyper-IgD) Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adult and pediatric patients, and Familial Mediterranean Fever (FMF) in adult and pediatric patients. Canakinumab is also indicated for the treatment of active Still's disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA) in patients ≥ 2 years of age.

Canakinumab is a human monoclonal anti-human IL-1β antibody approved by the U.S. Food and Drug Administration (FDA) in 2009 for the treatment of periodic fever syndromes and in 2020 for active Still's disease. It works by binding to human IL-1β and neutralizing its activity through blocking the interaction with IL-1 receptors. However, it does not bind IL-1α or IL-1 receptor antagonist (IL-1ra).

Periodic fever syndrome is a classification of autoinflammatory diseases, in which inflammation and recurrent fevers present as a result of antigen-independent immune system activation. Periodic fever syndromes include Cryopyrin-Associated Periodic Syndromes (CAPS) [including Familial Cold Auto-Inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS)], Familial Mediterranean Fever (FMF), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), and Tumor Necrosis Factor (TNF) Receptor-Associated Periodic Syndrome (TRAPS).

CAPS are rare genetic syndromes usually caused by mutations in the NLRP-3 gene, which encodes the cryopyrin protein. Cryopyrin is an important component of the inflammasome, and it regulates the protease caspase-1 and controls IL-1β activation. NLRP-3 mutations lead to an overactive inflammasome which results in excessive release of activated IL-1β, driving inflammation. Still's disease is a severe autoinflammatory disease, caused by innate immunity through proinflammatory cytokines like IL-1β. CAPS disorders are inherited via an autosomal dominant pattern. Three distinct phenotypes exist as a result of this genetic defect; however, each differs in severity and organ system affected. FCAS is a milder in severity and commonly present in the U.S., while MWS is intermediate in severity but more commonly identified in Europe. Common features of these disorders include fever, urticaria-like rash, joint pain, muscle pain, fatigue, and conjunctivitis.

FMF is a hereditary autoinflammatory disorder marked by recurrent episodes of fever and serosal inflammation, with secondary complication of amyloidosis that can lead to eventual renal failure

if not controlled. FMF is caused by a mutation in the MEFV gene encoding the protein pyrin, which assists in controlling the inflammatory system. The goal of therapy is to prevent acute attacks and minimize inflammation between attacks, and to prevent development and progression of amyloidosis. First-line treatment is with colchicine, and is recommended in all patients regardless of attack frequency and intensity. Interleukin-1 inhibitors is an alternative treatment for patients who do not respond to or cannot tolerate colchicine. Lack of response can be defined as frequent attacks despite receiving the maximally tolerated dose of colchicine for at least six months.

HIDS, which is now referred to as MKD, is a hereditary autosomal recessive disease associated with mevalonate kinase protein abnormality that in turn causes increased immunoglobulin levels. MKD is marked by episodes of high fever accompanied by skin rash, lymphadenopathy, joint pain, abdominal pain, vomiting and diarrhea. NSAIDs are used as first-line in symptomatic treatment of HIDS episodes, and glucocorticoids are typically used as second-line therapy in patients who fail NSAID treatment.

TRAPS is a rare genetic disorder characterized by recurrent episodes of fever and associated severe upper body muscle pain. TRAPS is caused by a defect in the *TNFR1* gene that encodes the 55 kDa receptor for tumor necrosis factor, which leads to an increase in normal inflammatory response. Development of amyloidosis can result from persistent, uncontrolled inflammation. While NSAIDs can help control fever in these patients, the standard treatment for attacks is glucocorticoid therapy. While there are no direct comparator trials available, IL-1 blockers have been shown to have more favorable efficacy than TNF inhibitors in the treatment of TRAPS, making them the preferred first-line biologic for treatment of this indication.

SJIA is a subset of JIA, and is defined within the American College of Rheumatology guidelines as arthritis in ≥ 1 joint for at least 6 weeks in a child < 16 years old with (or preceded by) a fever of at least a 2-week duration that is documented to be daily for at least 3 days and accompanied by one or more of the following: evanescent erythematous rash, generalized lymphadenopathy, hepatomegaly or splenomegaly, and serositis. The goal of SJIA therapy is to control active inflammation and symptoms, and to prevent morbidity related to the disease and/or treatment, such as joint damage, growth disturbances, and functional restrictions.

AOSD is a rare inflammatory disorder involving multiple systems that is marked by daily fever, arthritis, and evanescent rash. The underlying cause is unknown, and it can present as a monophasic, intermittent, or chronic course. Corticosteroids are used as first-line treatment for AOSD, and methotrexate is added to therapy in patients who are not controlled on corticosteroids alone. Refractory AOSD can be treated with TNF inhibitors, IVIG, anakinra, or IL-1 blockers.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for canakinumab (Ilaris®) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit

design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Canakinumab (Ilaris) is covered

Initial Therapy

Canakinumab (Ilaris) may be considered medically necessary when the following criteria are met:

1. The patient will be using canakinumab for treatment of one of the following indications:
    a. Cryopyrin-Associated Periodic Syndrome (CAPS) in patients 4 years of age and older, including Familial Cold Auto-Inflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS); OR
    b. Tumor Necrosis Factor (TNF) Receptor-Associated Periodic Syndrome (TRAPS); OR
    c. Hyperimmunoglobulin D Syndrome (HIDS) or Mevalonate Kinase Deficiency (MKD); OR
    d. Familial Mediterranean Fever (FMF), and one of the following:
        i. The patient has tried and had an inadequate response with colchicine for at least 6 months, or
        ii. The patient has a clinical contraindication or intolerance to colchicine; OR
    e. Active systemic juvenile idiopathic arthritis (SJIA), and all of the following:
        i. The patient is 2 years of age and older, and
        ii. The patient has documented active systemic features (e.g., ongoing fever for at least 2 weeks, evanescent erythematous rash, generalized lymphadenopathy, ≥1 joint with active arthritis, hepatomegaly, splenomegaly, serositis), and
        iii. One of the following:
            1. The patient has tried and had an inadequate response to two of the following drug classes:
                a. DMARDs (i.e., methotrexate, leflunomide) for at least a 3-month trial, or
                b. Systemic glucocorticoids (oral or IV) for at least a 3-month trial, or
                c. NSAIDs for at least a 1-month trial; or
            2. The patient has a clinical contraindication or intolerance to all of the drug classes listed above (i.e., DMARDs, systemic glucocorticoids, NSAIDs); or
            3. The patient has previously used another biologic immunomodulator agent indicated for the treatment of SJIA; OR
    f. Adult onset Still's disease (AOSD), and both of the following:
        i. One of the following:
            1. The patient has tried and had an inadequate response to at least one corticosteroid, or
            2. The patient has a clinical contraindication or intolerance to all corticosteroids, and
        ii. One of the following:
            1. The patient has tried and had an inadequate response to methotrexate, or
            2. The patient has a clinical contraindication or intolerance to methotrexate; AND

2. The patient will not be receiving canakinumab in combination with another biologic immunomodulator agent; AND
3. Canakinumab is prescribed by or in consultation with a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, pediatrician, rheumatologist).

Initial authorization: 12 months

Continuation Therapy

Continuation of treatment with canakinumab (Ilaris) beyond 12 months after initiation of therapy, and every 12 months thereafter, is considered medically necessary when the following criteria are met:

1. The patient is currently receiving canakinumab, and continues to meet or would have met initial criteria at the time of therapy initiation; AND
2. The patient has continued clinical benefit on canakinumab therapy; AND
3. The patient will not be receiving canakinumab in combination with another biologic immunomodulator agent; AND
4. Canakinumab is prescribed by or in consultation with a specialist in the area of the patient's diagnosis (e.g., allergist, immunologist, pediatrician, rheumatologist).

When Canakinumab (Ilaris) is not covered

Canakinumab (Ilaris) is considered **investigational** and therefore not covered when the above criteria are not met, and for all other indications not listed above.

Policy Guidelines

Ilaris is administered as a subcutaneous injection, which should be performed by a clinician. Ilaris is not intended for self-administration.

The recommended dosing regimen for Ilaris for each indication is as follows in the table below:

Indication	Dose (subcutaneous)	Frequency
CAPS (including FCAS and MWS)	Weight ≥15-40 kg: 2 mg/kg (inadequate response can increase to 3 mg/kg) Weight >40 kg: 150 mg	Every 8 weeks
TRAPS, HIDS/MKD, and FMF	Weight ≤40 kg: 2 mg/kg (inadequate response can increase to 4 mg/kg) Weight >40 kg: 150 mg (inadequate response can increase to 300 mg)	Every 4 weeks

Still's disease (AOSD and SJIA)	Weight ≥7.5 kg: 4 mg/kg (maximum of 300 mg)	Every 4 weeks

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *J0638*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

Novartis Pharmaceuticals Corporation. Ilaris (canakinumab) for injection for subcutaneous use. Highlights of prescribing information. June 2020. Available at: https://www.novartis.us/sites/www.novartis.us/files/ilaris.pdf. Last accessed September 2020.

Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis. American College of Rheumatology. October 2013. Arthritis & Rheumatism. 65(10):2499-2512.

Medical Director review 9/2020

Policy Implementation/Update Information

10/1/20 New policy developed. Ilaris is considered medically necessary for the treatment of patients with autoinflammatory periodic fever syndromes (CAPS, FCAS, MWS, TRAPS, HIDS, MKD, and FMF) and active Still's disease (AOSD and SJIA) when specified medical criteria and guidelines are met. Added HCPCS code J0638 to Billing/Coding section. References added. Medical Director review 9/2020. **Policy notification given 10/1/2020 for effective date 1/1/2021**. (krc)