09-J2000-03

Original Effective Date: 10/15/13

Reviewed: 03/12/25

Revised: 04/15/25

Subject: Canakinumab (Ilaris®) Injection

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

Dosage/ Administration	Position Statement	Billing/Coding	Reimbursement	Program Exceptions	Definitions
Related Guidelines	Other	References	Updates		

DESCRIPTION:

Canakinumab is a recombinant, human anti-human interleukin-1 beta (IL-1B) monoclonal antibody of the IgG1/kappa isotype. By binding to human IL-1B, canakinumab blocks the IL-1 receptor interaction and neutralizes overactive IL-1B activity which is present in disorders such as Cryopyrin-Associated Periodic Syndromes (CAPS) and systemic juvenile idiopathic arthritis (SJIA). Canakinumab does not bind IL-1 alpha or IL-1 receptor antagonist (IL-ra).

Cryopyrin-Associated Periodic Syndromes (CAPS) refer to rare genetic syndromes generally caused by mutations in the NLRP-3 [nucleotide-binding domain, leucine rich family (NLR), pyrin domain containing 3] gene (also known as Cold-Induced Auto-inflammatory Syndrome-1 [CIAS1]). CAPS disorders are inherited in an autosomal dominant pattern with male and female offspring equally affected. Features common to all disorders include fever, urticaria-like rash, arthralgia, myalgia, fatigue, and conjunctivitis.

The NLRP-3 gene encodes the protein cryopyrin, an important component of the inflammasome. Cryopyrin regulates the protease caspase-1 and controls the activation of interleukin-1 beta (IL-1β). Mutations in NLRP-3 result in an overactive inflammasome resulting in excessive release of activated IL-1β that drives inflammation. Systemic juvenile idiopathic arthritis (SJIA) is a severe auto-inflammatory disease, driven by innate immunity by means of pro-inflammatory cytokines such as interleukin 1β (IL-1β).

Canakinumab is FDA-approved for the treatment of CAPS including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 4 years of age and older. Canakinumab is also FDA-approved for the treatment of active Still's disease, including Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (SJIA) in patients aged 2 years and older, for the treatment of Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS),

Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), and Familial Mediterranean Fever (FMF).

On August 25, 2023 canakinumab was FDA approved for the treatment of gout flares in adults in whom non-steroidal anti-inflammatory drugs (NSAIDs) and colchicine are contraindicated, are not tolerated, or do not provide an adequate response, and in whom repeated courses of corticosteroids are not appropriate. The approval was based on three 12-week, randomized, double-blind, active-controlled studies in patients who met the aforementioned FDA-approved indication and experienced at least three gout flares in the previous year. Collectively among the three trials, 624 patients received canakinumab 150 mg subcutaneously and 361 patients received triamcinolone acetonide 40 mg intramuscularly. The study endpoints demonstrated lower pain intensity of the most affected joint at 72 hours post-dose and reduced the time to new flare over 12 weeks from randomization for the canakinumab group as compared to the triamcinolone group.

POSITION STATEMENT:

I. Initiation of canakinumab (Ilaris) **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Cryopyrin-Associated Periodic Syndrome (CAPS) or Cold Induced Auto-inflammatory Syndrome (CAIS) including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS)
    a. There is clinical documentation of functional impairment resulting in limitations of activities of daily living
    b. Canakinumab is **NOT** being administered in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Opzelura (ruxolitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
    c. The dose does not exceed 150 mg every 8 weeks
    d. The member is 4 years of age and older.
2. Active Still's disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA) (Pediatric Still's Disease)
    a. Member's disease is moderately to severely active
    b. Member had an inadequate response to a sufficient trial or a contraindication to **BOTH** of the following[†]:
        i. DMARD (e.g., methotrexate, leflunomide)
        ii. Systemic corticosteroids
    c. Canakinumab is **NOT** being administered in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant

(baricitinib), Rinvoq (upadacitinib), Opzelura (ruxolitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]

d. The dose does not exceed 300 mg every 4 weeks

e. Member is 2 years of age or older

3. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)
    a. Member has chronic or recurrent disease activity
    b. Canakinumab is **NOT** being administered in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Opzelura (ruxolitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
    c. The dose does not exceed 300 mg every 4 weeks
    d. Member is 2 years of age or older
4. Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
    a. Member has a diagnosis of HIDS with mevalonate kinase deficiency and a history of flares
    b. Canakinumab is **NOT** being administered in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Opzelura (ruxolitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
    c. The dose does not exceed 300 mg every 4 weeks
    d. Member is 2 years of age or older
5. Familial Mediterranean Fever (FMF)
    a. Member had an inadequate response or contraindication to colchicine
    b. Canakinumab is **NOT** being administered in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Opzelura (ruxolitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
    c. The dose does not exceed 300 mg every 4 weeks
    d. Member is 2 years of age or older

6. Gout Flares
    a. Member has experienced 3 or more gout flares within the previous 12 months
    b. Acute gout flares are unresponsive to maximum FDA-labeled doses of NSAIDs, colchicine, and corticosteroids, unless an intolerance or contraindication is present – Documentation must be submitted
    c. Serum uric acid levels are greater than 6 mg/dL despite maximized chronic gout therapies (e.g., xanthine oxidase inhibitor and a uricosuric agent such as probenecid) – Documentation must be submitted
    d. Canakinumab is **NOT** being administered in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Opzelura (ruxolitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)]
    e. The dose does not exceed 150 mg subcutaneous every 12 weeks
    f. Member is 18 years of age or older

Duration of approval: 12 months

II. Continuation of canakinumab (Ilaris) injection **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:
    1. Member has a history of beneficial clinical response with canakinumab therapy for the treatment of **ONE** of the following indications:
        a. Cryopyrin-Associated Periodic Syndrome (CAPS) or Cold Induced Auto-inflammatory Syndrome (CAIS) including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS)
        b. Active Still's disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA) (Pediatric Still's Disease)
        c. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)
        d. Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
        e. Familial Mediterranean fever (FMF)
        f. Gout flares
    2. The member has been previously approved by Florida Blue or another health plan in the past 2 years (if another health plan, documentation of a health plan-paid claim during the 90 days before the authorization request must be submitted), **OR** the member has previously met all indication-specific criteria.
    3. Canakinumab is **NOT** being administered in combination with another biologic immunomodulator agent (full list in "Other" section); Janus kinase (JAK) inhibitor [Cibinqo (abrocitinib), Leqselvi (deuruxolitinib), Litfulo (ritlecitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Opzelura (ruxolitinib), Xeljanz (tofacitinib), and Xeljanz XR (tofacitinib extended

release)]; Otezla (apremilast); Sotyktu (deucravacitinib); or sphingosine-1-phosphate (S1P) modulator [Velsipity (etrasimod) and Zeposia (ozanimod)].

4. The dose does not exceed the following based on indication:
    a. Cryopyrin-Associated Periodic Syndrome (CAPS) or Cold Induced Auto-inflammatory Syndrome (CAIS) including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS): 150 mg subcutaneous every 8 weeks
    b. Active Still's disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA) (Pediatric Still's Disease): 300 mg subcutaneous every 4 weeks
    c. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS), Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD), or Familial Mediterranean Fever (FMF): 300 mg subcutaneous every 4 weeks
    d. Gout flares: 150 mg subcutaneous every 12 weeks

Duration of approval: 12 months

†Step not required if the member previously had an inadequate response to an alternative biologic

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

Cryopyrin-Associated Periodic Syndromes

- Body weight greater than 40 kg: 150 mg subcutaneously every 8 weeks
- Body weight greater than or equal to 15 kg and less than or equal to 40 kg: 2 mg/kg (may increase to 3 mg/kg if inadequate response) subcutaneously every 8 weeks

Active Still's disease, including Adult-Onset Still's Disease (AOSD) and Systemic Juvenile Idiopathic Arthritis (SJIA)

- 4 mg/kg (maximum of 300 mg; body weight greater than or equal to 7.5 kg) subcutaneously every 4 weeks

Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)

- Body weight greater than 40 kg: 150 mg subcutaneously every 4 weeks (may increase to 300 mg every 4 weeks if the clinical response is not adequate)
- Body weight less than or equal to 40 kg: 2 mg/kg administered every 4 weeks (may increase to 4 mg/kg every 4 weeks if the clinical response is not adequate)

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

- Body weight greater than 40 kg: 150 mg subcutaneously every 4 weeks (may increase to 300 mg every 4 weeks if the clinical response is not adequate)

- Body weight less than or equal to 40 kg: 2 mg/kg administered every 4 weeks (may increase to 4 mg/kg every 4 weeks if the clinical response is not adequate)

Familial Mediterranean Fever (FMF)

- Body weight greater than 40 kg: 150 mg subcutaneously every 4 weeks (may increase to 300 mg every 4 weeks if the clinical response is not adequate)
- Body weight less than or equal to 40 kg: 2 mg/kg administered every 4 weeks (may increase to 4 mg/kg every 4 weeks if the clinical response is not adequate)

Gout Flares

- 150 mg subcutaneously every 12 weeks

Dose Adjustments

None

Drug Availability

- 150 mg/ml single-use, glass vial

PRECAUTIONS:

Boxed Warning

None

Contraindications

- Confirmed hypersensitivity to the active substance or to any of the excipients

Precautions/Warnings

- Interleukin-1 blockade may interfere with immune response to infections; discontinue treatment if serious or active infection
- Live vaccines should not be given concurrently
- It is unknown if treatment with immunosuppressants such as anti-interleukin-1 therapy result in an increased risk of malignancy.
- Hypersensitivity reactions have occurred.
- Macrophage activation syndrome (MAS) is a known, life-threatening disorder that may develop in patients with rheumatic conditions and should be aggressively treated. Prescribers should be attentive to symptoms of infection or worsening SJIA.

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J0638	Injection, canakinumab, 1 mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

D89.89	Other specified disorders involving the immune mechanism, not elsewhere classified
E85.0	Non-neuropathic heredofamilial amyloidosis
L50.2	Urticaria due to cold and heat
M04.1	Periodic fever syndrome
M04.2	Cryopyrin-associated periodic syndromes
M04.8	Other autoinflammatory syndromes
M04.9	Autoinflammatory syndrome, unspecified
M06.1	Adult-onset Still's disease
M08.00 – M.08.09	Unspecified juvenile rheumatoid arthritis of unspecified sites
M08.0A	Unspecified juvenile rheumatoid arthritis, other specified site
M08.1	Juvenile ankylosing spondylitis
M08.20 – M08.29	Juvenile rheumatoid arthritis with systemic onset, unspecified sites
M08.2A	Juvenile rheumatoid arthritis with systemic onset, other specified site
M08.3	Juvenile rheumatoid polyarthritis (seronegative)
M08.40 – M08.48	Pauciarticular juvenile rheumatoid arthritis, unspecified sites
M08.4A	Pauciarticular juvenile rheumatoid arthritis, other specified site
M08.80 – M08.89	Other juvenile arthritis, unspecified sites
M08.90 – M08.99	Juvenile arthritis, unspecified, unspecified sites
M08.9A	Juvenile arthritis, unspecified, other specified site
M10.00 – M10.09	Idiopathic gout
M10.311 – M10.39	Gout due to renal impairment
M10.40 – M10.49	Other secondary gout
M10.9	Gout, unspecified
M35.9	Systemic involvement of connective tissue, unspecified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time this guideline was drafted.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if

based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Cryopyrin-Associated Periodic Syndrome (CAPS) aka Cold Induced Auto-inflammatory Syndrome (CAIS1): is a spectrum of auto-inflammatory syndromes including familial cold auto-inflammatory syndrome (FCAS, formerly termed familial cold-induced urticaria), the Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disease (NOMID, also called chronic infantile neurologic cutaneous and articular syndrome or CINCA).

DMARD: Disease-modifying antirheumatic drug

Familial cold auto-inflammatory syndrome (FCAS): is an autosomal dominant condition characterized by rash, conjunctivitis, fever/chills and arthralgias elicited by exposure to cold.

Familial Mediterranean fever (FMF): is an inherited autosomal recessive condition characterized by recurrent episodes of painful inflammation in the abdomen, chest, joints, muscles, scrotum or skin accompanied by fever.

Hyperimmunoglobulin D syndrome (HIDS): is a rare inherited autosomal recessive condition characterized by recurrent episodes of fever associated with painful inflammation in the abdomen or joints and skin rash. The condition is associated with decreased activity of mevalonate kinase (MVK).

Macrophage Activation Syndrome (MAS): a life-threatening condition characterized by fever, organomegaly, cytopenias, hyperferritinemia, hypertriglyceridemia, hypofibrinogenemia, coagulopathy, and other symptoms.

Muckle-Wells syndrome (MWS): is a rare autosomal dominant disease which causes sensorineural deafness, recurrent hives, and can lead to amyloidosis.

Neonatal-onset multisystem inflammatory disease (NOMID) or chronic infantile neurologic cutaneous and articular syndrome or CINCA: is a rare genetic periodic fever syndrome which causes uncontrolled inflammation in multiple parts of the body starting in the newborn period.

Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS): a rare genetic disease with episodes of recurrent fever, abdominal, chest and muscle pain and a typical rash lasting for more than one week.

RELATED GUIDELINES:

Rilonacept (Arcalyst®) Injection, 09-J2000-04

OTHER:

NOTE: The list of biologic immunomodulator agents not permitted as concomitant therapy can be found at 09-J9000-02, Biologic Immunomodulator Agents Not Permitted as Concomitant Therapy.

REFERENCES:

1. AHFS Drug Information. Bethesda (MD): American Society of Health-System Pharmacists, Inc; 2016 [cited 2016 Aug 17]. In: STAT! Ref Online Electronic Medical Library [Internet]. Available from: http://online.statref.com/.
2. Clinical Pharmacology [Internet]. Tampa (FL): Gold Standard, Inc.; 2025 [cited 2025 February 25]. Available from: http://www.clinicalpharmacology.com/.
3. DRUGDEX® System [Internet]. Greenwood Village (CO): Thomson Micromedex; Updated periodically [cited 2025 February 25]. Available from: www.micromedexsolutions.com/.
4. FDA Orphan Drug Designations and Approvals [Internet]. Washington, D.C. [cited 2025 February 25]. Available from: http://www.accessdata.fda.gov/scripts/opdlisting/oopd/.
5. Ilaris® [package insert]. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; November 2024.
6. Lachmann HJ, Kone-Paut I, Kuemmerle-Deschner JB et al. Use of canakinumab in the cryopyrin-associated periodic syndrome. N Engl J Med. 2009; 360: 2416-2425.
7. 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: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. Arthritis Rheum. 2013; 65: 2499-2512.
8. Ringold S, Angeles-Han ST, Beukelman T et al. 2019 American College of Rheumatology/Arthritis Foundation Guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for non-systemic polyarthritis, arcroilitis, and enthesitis. Arthritis Rheum. 2019; 71: 717-734.
9. Ruperto N, Brunner HI, Quartier P et al. Two randomized trials of canakinumab in systemic juvenile idiopathic arthritis. N Engl J Med. 2012; 367: 2396-2406.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Coverage Committee on 03/12/25.

GUIDELINE UPDATE INFORMATION:

10/15/13	New Medical Coverage Guideline.
10/15/14	Review and revision to guideline; consisting of revising position statement, dosage/administration, precautions/warnings, coding, references.
10/15/15	Review and revision to guideline; consisting of revising position statement, precautions/warnings, definitions, coding, references.
11/01/15	Revision: ICD-9 Codes deleted.
10/01/16	Update to ICD-10 codes.
10/15/16	Review and revision to guideline; consisting of revising position statement, definitions, coding, references.
11/15/16	Revision to guideline; consisting of updating position statement and references.
08/15/20	Revision to guideline; consisting of updating position statement, description, dosing, coding and references.
10/01/20	Revision to ICD-10 coding.

04/15/23	Review and revision of the guideline, consisting of updating the position statement to include additional interleukin blockers that are not permitted as concomitant therapy and to require documentation from other health plans for continuation and updating the references.
12/15/23	Review and revision of the guideline, consisting of revising the position statement to include the indication for acute gout flares unresponsive to maximum FDA-labeled doses of NSAIDs, colchicine, and corticosteroids, unless an intolerance or contraindication is present and updating biologics not permitted as concomitant therapy, dosing, billing/codes, and references.
04/15/24	Revision to guideline; consisting of updating references.
04/15/25	Revision to the guideline consisting of revising the position statement to add Leqselvi (deuruxolitinib) to the JAK inhibitor list not to use in combination with canakinumab (Ilaris), adding the policy that lists the biologics not permitted as concomitant therapy in the Other section, and updating the references.