Oscar Clinical Guideline: Ilaris (canakinumab) (PG185, Ver. 1)

Ilaris (canakinumab)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Ilaris (canakinumab) is a human monoclonal antibody against interleukin (IL)-1 beta approved for the treatment of several auto-inflammatory diseases characterized by recurrent fever and inflammation. Ilaris (canakinumab) is indicated for:

1. the treatment of the following autoinflammatory Periodic Fever Syndromes:
    a. Cryopyrin-Associated Periodic Syndromes (CAPS), in adults and pediatric patients 4 years of age and older, including:
        i. Familial Cold Autoinflammatory Syndrome (FCAS)
        ii. Muckle-Wells Syndrome (MWS)
    b. Familial Mediterranean Fever (FMF) in adult and pediatric patients.
    c. Hyperimmunoglobulin D (Hyper-IgD) Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adult and pediatric patients.
    d. Tumor Necrosis Factor (TNF) Receptor Associated Periodic Syndrome (TRAPS) in adult and pediatric patients.

2. 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 and older.
3. the symptomatic treatment of adult patients with gout flares 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.

Ilaris (canakinumab) blocks the proinflammatory cytokine IL-1β, a key driver of inflammation in these diseases. By neutralizing IL-1β, Ilaris (canakinumab) prevents attacks, reduces pain, and controls disease activity. For gout flares specifically, canakinumab reduces pain, risk of new flares, and the need for corticosteroids compared to other options when they are contraindicated or ineffective. Guidelines recommend considering IL-1 blockers like canakinumab for frequent gout flares if other treatments fail.

Definitions

"**Adult-Onset Still's Disease (AOSD)**" is a rare autoinflammatory disorder similar to SJIA, typically occurring in young adults, characterized by high spiking fevers, evanescent rash, and arthritis.

"**Cryopyrin-Associated Periodic Syndromes (CAPS)**" refers to a group of rare autoinflammatory conditions caused by mutations in the NLRP3 gene, leading to overproduction of interleukin-1 beta (IL-1ß). Includes conditions such as Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS).

"**Familial Mediterranean Fever (FMF)**" is a hereditary autoinflammatory condition characterized by recurrent episodes of fever and serositis causing pain in the abdomen, chest, joints or skin. Caused by mutations in the MEFV gene.

"**Hyperimmunoglobulin D Syndrome (HIDS)**" is an autosomal recessive autoinflammatory condition caused by mutations in the MVK gene causing deficiency of the enzyme mevalonate kinase. Leads to recurrent fever episodes associated with lymphadenopathy, arthralgia, gastrointestinal distress and skin rashes. Also known as "Mevalonate Kinase Deficiency (MKD)."

"**Systemic Juvenile Idiopathic Arthritis (SJIA)**" is a severe autoinflammatory arthritis occurring in children, driven by innate immunity and overproduction of inflammatory cytokines like interleukin-1 beta (IL-1ß).

"**Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)**" refers to a rare autosomal dominant autoinflammatory condition caused by mutations in the TNFRSF1A gene causing prolonged inflammatory attacks and fever episodes.

Medical Necessity Criteria for Initial Authorization

The Plan considers **Ilaris (canakinumab)** medically necessary when **ALL** of the following criteria are met:

General Criteria *(applicable to all indications)*:

1. Prescribed by or in consultation with a rheumatologist, immunologist, allergist, or other specialist relevant to the clinical indication; ***AND***
2. Age and dosing are in accordance with FDA-approved labeling **OR** are supported by evidence-based treatment guidelines for the requested indication:
    a. Cryopyrin-Associated Periodic Syndromes (CAPS) - 4 years of age and older.
    b. Familial Mediterranean Fever (FMF) - 2 years of age and older.
    c. Gout Flares - adults, 18 years of age and older.
    d. Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) - 2 years of age and older.
    e. Still's Disease (Adult-Onset Still's Disease [AOSD] and Systemic Juvenile Idiopathic Arthritis [SJIA]) - 2 years of age and older.
    f. Tumor Necrosis Factor Receptor (TNF) Associated Periodic Syndrome (TRAPS) - 2 years of age and older; ***AND***
3. Documentation provided confirms the following:
    a. A negative TB skin test (IGRA or PPD) within the past 6 months.
    b. The member does not have an active infection.
    c. The member will **NOT** be using Ilaris (canakinumab) concomitantly with tumor necrosis factor (TNF) inhibitors (e.g., adalimumab, certolizumab, etanercept, golimumab, inFLIXimab, lenalidomide, pomalidomide, thalidomide); ***AND***
4. Diagnosis and indication-specific criteria are met, as outlined below:

Additional Criteria by Indication:

Adult-Onset Still's Disease

5. Diagnosis of Adult-Onset Still's Disease; ***AND***
6. Quotidian (a daily recurring fever) or double-quotidian (two fever spikes per day) is present; ***AND***
7. Active articular disease with at least 4 swollen **AND** 4 tender joints; ***AND***
8. The member is unable to use, or has tried and failed **BOTH** of the following:

a. At least **ONE** of the following:
    i. nonsteroidal antiinflammatory drugs (NSAIDs), such as naproxen; ***or***
    ii. glucocorticoids (e.g., prednisone); ***or***
    iii. disease-modifying antirheumatic drugs (DMARDs), such as methotrexate; ***and***
b. Kineret (anakinra).

<u>Cryopyrin-Associated Periodic Syndromes</u>

5. Diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS); ***AND***
6. Documentation of NLRP3/CIAS1 gene mutation confirmation; ***AND***
7. The member is unable to use, or has tried and failed Kineret (anakinra).

<u>Familial Mediterranean Fever (FMF)</u>

6. Diagnosis of Familial Mediterranean Fever (FMF); ***AND***
7. Documentation of MEFV gene mutation; ***AND***
8. The member is unable to use, or has tried and failed **BOTH** of the following:
    a. Colchicine (at maximum tolerated doses); ***and***
    b. Kineret (anakinra).

<u>Gout Flares</u>

5. Diagnosis of acute gout flares; ***AND***
6. History of frequent gout flares, defined as 2 or more flares within the past 12 months; ***AND***
7. The member is unable to use, or has tried and failed ALL of the following:
    a. NSAIDs (at maximum tolerated doses), such as naproxen; ***and***
    b. Colchicine; ***and***
    c. glucocorticoids (e.g., prednisone); ***and***
    d. Kineret (anakinra); ***AND***
8. Requested dose is 150 mg subcutaneously as a single dose, with repeat doses at intervals of at least 12 weeks.

<u>Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)</u>

5. Diagnosis of Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD); ***AND***
6. Documentation of elevated serum IgD level OR genetic test confirming MVK gene mutation; ***AND***
7. The member is unable to use, or has tried and failed Kineret (anakinra).

Systemic Juvenile Idiopathic Arthritis

5. Diagnosis of Systemic Juvenile Idiopathic Arthritis; ***AND***
6. Active systemic disease defined as ≥2 weeks of documented fever AND ≥2 joints with active arthritis; ***AND***
7. The member is unable to use, or has tried and failed **BOTH** of the following:
    a. NSAIDs or glucocorticoids; ***and***
    b. Kineret (anakinra).

Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)

5. Diagnosis of Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS); ***AND***
6. Documentation of genetic test confirming TNFRSF1A mutation; ***AND***
7. The member is unable to use, or has tried and failed Kineret (anakinra).

If the above prior authorization criteria are met, Ilaris (canakinumab) will be authorized for 6-months.

Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if the member has recent (within the last 3 months) clinical chart documentation demonstrating ALL of the following criteria:

1. Prescribed by or in consultation with a rheumatologist, immunologist, allergist, or other specialist relevant to the clinical indication; ***AND***
2. Documentation shows a positive clinical response compared to pretreatment baseline, defined as improvement in signs and symptoms; ***AND***

    Additionally, for Gout Flares:
3. Time interval since the most recent Ilaris dose is at least 12 weeks; ***AND***
4. The currently requested dose does not exceed 150 mg.

Experimental or Investigational / Not Medically Necessary

Ilaris (canakinumab) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

Applicable Billing Codes (HCPCS/CPT Codes)

Service(s) name	
CPT/HCPCS Codes considered medically necessary if criteria are met:	
Code	*Description*
J0638	Injection, canakinumab, 1 mg
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
ICD-10 codes considered medically necessary if criteria are met:	
Code	*Description*
M04.1	Periodic fever syndromes
M04.2	Cryopyrin-associated periodic syndromes
M06.1	Adult-onset Still's disease
M08.20	Juvenile rheumatoid arthritis with systemic onset, unspecified site
M08.211	Juvenile rheumatoid arthritis with systemic onset, right shoulder
M08.212	Juvenile rheumatoid arthritis with systemic onset, left shoulder
M08.219	Juvenile rheumatoid arthritis with systemic onset, unspecified shoulder
M08.22	Juvenile rheumatoid arthritis with systemic onset, elbow
M08.221	Juvenile rheumatoid arthritis with systemic onset, right elbow
M08.222	Juvenile rheumatoid arthritis with systemic onset, left elbow
M08.229	Juvenile rheumatoid arthritis with systemic onset, unspecified elbow
M08.231	Juvenile rheumatoid arthritis with systemic onset, right wrist
M08.232	Juvenile rheumatoid arthritis with systemic onset, left wrist
M08.239	Juvenile rheumatoid arthritis with systemic onset, unspecified wrist
M08.241	Juvenile rheumatoid arthritis with systemic onset, right hand
M08.242	Juvenile rheumatoid arthritis with systemic onset, left hand
M08.249	Juvenile rheumatoid arthritis with systemic onset, unspecified hand
M08.251	Juvenile rheumatoid arthritis with systemic onset, right hip
M08.252	Juvenile rheumatoid arthritis with systemic onset, left hip

M08.259	Juvenile rheumatoid arthritis with systemic onset, unspecified hip
M08.261	Juvenile rheumatoid arthritis with systemic onset, right knee
M08.262	Juvenile rheumatoid arthritis with systemic onset, left knee
M08.269	Juvenile rheumatoid arthritis with systemic onset, unspecified knee
M08.271	Juvenile rheumatoid arthritis with systemic onset, right ankle and foot
M08.272	Juvenile rheumatoid arthritis with systemic onset, left ankle and foot
M08.279	Juvenile rheumatoid arthritis with systemic onset, unspecified ankle and foot
M08.28	Juvenile rheumatoid arthritis with systemic onset, vertebrae
M08.29	Juvenile rheumatoid arthritis with systemic onset, multiple sites
M10.9	Gout, unspecified

References

1. Arostegui JI, Anton J, Calvo I, et al. Long-term efficacy and safety of canakinumab in active hyper-IgD syndrome (HIDS): results from an open-label study. Pediatric Rheumatology. 2015;13(supp 1):58.
2. Babaoglu H, Varan O, Kucuk H, et al. Effectiveness of canakinumab in colchicine- and anakinra-resistant or -intolerant adult familial mediterranean fever patients: a single-center real-life study. J Clin Rheumatol. 2020;26(1):7-13. doi:10.1097/RHU.0000000000000873
3. Bilgin E., et al.: Proposal for a simple algorithm to differentiate adult-onset Still's disease with other fever of unknown origin causes: a longitudinal prospective study . Clin Rheum 2019; 38 (6): pp. 1699.
4. Bodard Q et al: Cardiac involvement in adult-onset Still's disease: manifestations, treatments and outcomes in a retrospective study of 28 patients, J Autoimmun 116, 2021.
5. Brik R, Butbul-Aviel Y, Lubin S, et al. Canakinumab for the treatment of children with colchicine-resistant familial Mediterranean fever: a 6-month open-label, single-arm pilot study. Arthritis Rheumatol. 2014;66(11):3241-3243.
6. De Benedetti F, Gattorno M, Anton J, et al. Canakinumab for the treatment of autoinflammatory recurrent fever syndromes. N Engl J Med. 2018;378(20):1908-1919. doi:10.1056/NEJMoa1706314
7. Efficacy of Canakinumab in Patients With Cryopyrin-Associated Periodic Syndrome Across Different Severity Phenotypes," Ann Rheum Dis, 2011, 70(12):2095-102.
8. Furst DE, Keystone EC, Braun J, et al, "Updated Consensus Statement on Biological Agents for the Treatment of Rheumatic Diseases, 2010," Ann Rheum Dis, 2011, 70(Suppl 1)2-36.
9. Hu Q., et al.: Increased neutrophil extracellular traps activate NLRP3 and inflammatory macrophages in adult-onset Still's disease . Arthritis Res Ther 2019; 21 (1): pp. 1-11.
10. Ilaris (canakinumab) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; August 2023.
11. Jamilloux Y., et al.: Treatment of adult-onset Still's disease: a review . Ther Clin Risk Manag 2015; 11: pp. 33.

12. Kiltz U., et al.: Prolonged treatment with tadekinig alfa in adult-onset Still's disease . Ann Rheum Dis 2020; 79 (1): pp. e10.
13. 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(23):2416-25.
14. Mitrovic S., Fautrel B.: New markers for adult-onset Still's disease . Joint Bone Spine 2018; 85 (3): pp. 285.
15. Ozen S, Demirkaya E, Erer B, et al. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis. 2016;75(4):644-651. doi:10.1136/annrheumdis-2015-208690
16. Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. Ann Rheum Dis. 2017;76(1):29-42. doi: 10.1136/annrheumdis-2016-209707.
17. Ruperto N, Brunner H, Horneff G, et al, "Efficacy and Safety of Canakinumab, a Long Acting Fully Human Anti-Interleukin-1ß Antibody, in Systemic Juvenile Idiopathic Arthritis With Active Systemic Features: Results From a Phase III Study," Pediatric Rheumatology, 2011, 9(Suppl 1):021.
18. Ruperto N, Brunner HI, Quartier P, et al, "Two Randomized Trials of Canakinumab in Systemic Juvenile Idiopathic Arthritis," N Engl J Med, 2012, 367(25):2396-406.
19. Ruscitti R., et al.: Adult-onset Still's disease: evaluation of prognostic tools and validation of the systemic score by analysis of 100 cases from 3 centers . BMC Med 2016; 14: pp. 194.
20. Sibley CH, Chioato A, Felix S, et al. A 24 month open-label study of canakinumab in neonatal-onset multisystem inflammatory disease. Ann Rheum Dis. 2015;74(9):1714-1719.

Clinical Guideline Revision / History Information

Original Date: 12/14/2023
Reviewed/Revised: