MEDICAL MUTUAL®

Drug Policy

Policy:	**201703**	**Initial Effective Date: 02/14/2017**
Code(s):	**HCPCS J0638**	**Annual Review Date: 10/19/2023**
SUBJECT:	**Ilaris® (canakinumab)**	**Last Revised Date: 10/19/2023**

☒Subject to Site of Care

Prior approval is required for some or all procedure codes listed in this Corporate Drug Policy.

Initial and renewal requests for the medication(s) listed in this policy are subject to site of care management. When billed under the medical benefit, administration of the medication will be restricted to a non-hospital facility-based location (i.e., home infusion provider, provider's office, free-standing ambulatory infusion center) unless the member meets the site of care exception criteria. To view the exception criteria and a list of medications subject to site of care management please click here.

POLICY STATEMENT

This policy involves the use of Ilaris. Prior authorization is recommended for medical benefit coverage of Ilaris. Approval is recommended for those who meet the conditions of coverage in the **Criteria, Dosing, Initial/Extended Approval, Duration of Therapy**, and **Labs/Diagnostics** for the diagnosis provided. **Waste Management** applies for all covered conditions that are administered by a healthcare professional. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria and Waste Management section. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Ilaris as well as the monitoring required for AEs and long-term efficacy, initial approval requires Ilaris be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

All reviews for use of Ilaris for COVID-19 and/or cytokine release syndrome associated with COVID-19 will be forwarded to the Medical Director.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Ilaris is recommended in those who meet the following criteria:

1. The patient will not use Ilaris concurrently with other biologics AND;

2. Ilaris will not be used to treat Rhematoid Arthritis [RA] AND;

FDA-Approved Indications

1. Cryopyrin-Associated Periodic Syndromes (CAPS) (including Familial Cold Autoinflammatory Syndrome [FCAS], Muckle-Wells Syndrome [MWS], and Neonatal Onset Multisystem Inflammatory Disease [NOMID] or Chronic Infantile Neurological Cutaneous and Articular [CINCA] Syndrome).

A) Initial Therapy. Approve for 6 months if the patient meets the following conditions (i, ii, and iii):

i. Patient is ≥ 4 years of age; AND

ii. Ilaris is prescribed by or in consultation with a rheumatologist, geneticist, allergist/immunologist, or dermatologist; AND

iii. Genetic test to show mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1, also known as NLRP3)

B) Patient is Currently Receiving Ilaris. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, amyloid A), reduction in proteinuria, and/or stabilization of serum creatinine.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as fewer cold-induced attacks; less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

Dosing
Patient > 40 kg: 150 mg administered subcutaneously (SC) every 8 weeks.
Patients ≥ 15 kg and ≤ 40 kg: 2 mg/kg SC every 8 weeks
For children with body weight 15 to 40 kg WITH inadequate response to initial treatment, dosage of 3mg/kg may be initiated

2. Familial Mediterranean Fever (FMF).

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, iv, and v):

i. Patient is ≥ 2 years of age; AND

ii. Patient has tried colchicine, unless contraindicated; AND

iii. Patient will be taking Ilaris in combination with colchicine, unless colchicine is contraindicated or not tolerated; AND

iv. Prior to starting Ilaris, the patient meets both of the following (a and b):

a) C-reactive protein level is ≥ 10 mg/L OR elevated to at least two times the upper limit of normal for the reporting laboratory; AND

b) Patient has a history of at least one flare per month despite use of colchicine, OR was hospitalized for a severe flare; AND

v. The medication is prescribed by or in consultation with a rheumatologist, nephrologist, geneticist, gastroenterologist, oncologist, or hematologist.

B) Patient is Currently Receiving Ilaris. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include decreased frequency of attacks, resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, amyloid A), reduction in proteinuria, and/or stabilization of serum creatinine.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

Dosing:
Patient ≤ 40 kg: Start at 2 mg/kg every 4 weeks. The dose can be increased to 4 mg/kg every 4 weeks, if clinical response is not adequate.
Patient > 40 kg: start at 150 mg every 4 weeks. The dose can be increased to 300mg every 4 weeks if clinical response is not adequate.

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

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is ≥ 2 years of age; AND

ii. Prior to starting Ilaris, the patient meets both of the following (a and b):

a) C-reactive protein level is ≥ 10 mg/L OR elevated to at least two times the upper limit of normal for the reporting laboratory; AND

b) Patient has a history of at least three febrile acute flares within the previous 6-month period OR was hospitalized for a severe flare; AND

iii. The medication is prescribed by or in consultation with a rheumatologist, nephrologist, geneticist, oncologist, or hematologist.

B) Patient is Currently Receiving Ilaris. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR

Note: Examples of objective measures include decreased frequency of attacks, resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, amyloid A), reduction in proteinuria, and/or stabilization of serum creatinine.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

Dosing:
Patient ≤ 40 kg: Start at 2 mg/kg every 4 weeks. The dose can be increased to 4 mg/kg every 4 weeks, if clinical response is not adequate. (2.3)
Patient > 40 kg: start at 150 mg every 4 weeks. The dose can be increased to 300mg every 4 weeks if clinical response is not adequate.

4. Stills Disease, Adult Onset. Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months (which is adequate for three doses) if the patient meets ALL of the following conditions (i, ii, and iii):

i. Patient is ≥ 18 years of age; AND
Note: If the patient is < 18 years of age, refer to criteria for systemic juvenile idiopathic arthritis.

ii. Patient meets ONE of the following conditions (a, b, or c):

a) Patient has tried at least TWO other biologics; OR
Note: Examples of biologics include Actemra (tocilizumab intravenous infusion, tocilizumab subcutaneous injection), Kineret (anakinra subcutaneous injection), Orencia (abatacept intravenous infusion, abatacept subcutaneous injection), an etanercept product, adalimumab product, or infliximab product.

b) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient has features of poor prognosis, as determined by the prescriber; AND
Note: Examples of features of poor prognosis include arthritis of the hip, radiographic damage, 6-month duration of significant active systemic disease, defined by: fever, elevated inflammatory markers, or requirement for treatment with systemic glucocorticoids.

(2) Patient has tried Actemra or Kineret; OR

c) Patient meets BOTH of the following [(1) and (2)]:

(1) Patient has active systemic features with concerns of progression to macrophage activation syndrome, as determined by the prescriber; AND

(2) Patient has tried Kineret; AND

iii. Ilaris is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Ilaris. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

Dosing:
Patients ≥ 7.5kg: 4 mg/kg (with a maximum of 300 mg) subcutaneously every 4 weeks

5. **Systemic Juvenile Idiopathic Arthritis (SJIA).** Approve for the duration noted if the patient meets ONE of the following (A or B):

A) Initial Therapy. Approve for 6 months (which is adequate for three doses) if the patient meets ALL of the following conditions (i, ii, and iii):

i. Patient is ≥ 2 years of age; AND

ii. Patient meets ONE of the following conditions (a, b, or c):

a) Patient has tried at least TWO other biologics; OR
Note: Examples of biologics for SJIA include Actemra (tocilizumab intravenous infusion, tocilizumab subcutaneous injection), Kineret (anakinra subcutaneous injection), Orencia (abatacept intravenous infusion, abatacept subcutaneous injection), an etanercept product, adalimumab product, or infliximab product.

b) Patient meets BOTH of the following [(1) and (2)]:
a) Patient has features of poor prognosis, as determined by the prescriber; AND
Note: Examples of features of poor prognosis include arthritis of the hip, radiographic damage, 6-month duration of significant active systemic disease, defined by: fever, elevated inflammatory markers, or requirement for treatment with systemic glucocorticoids.
b) Patient has tried Actemra or Kineret; OR

c) Patient meets BOTH of the following [(1) and (2)]:
a) Patient has features of SJIA with active systemic features with concerns of progression to macrophage activation syndrome, as determined by the prescriber; AND
b) Patient has tried Kineret; AND

iii. Ilaris is prescribed by or in consultation with a rheumatologist.

B) Patient is Currently Receiving Ilaris. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR

Note: Examples of objective measures include resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), and/or reduced dosage of corticosteroids.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

Dosing:
Patients ≥ 7.5kg: 4 mg/kg (with a maximum of 300 mg) subcutaneously every 4 weeks

6. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS).

A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

i. Patient is ≥ 2 years of age; AND

ii. Prior to starting Ilaris, the patient meets both of the following (a and b):

a) C-reactive protein level is ≥ 10 mg/L OR elevated to at least two times the upper limit of normal for the reporting laboratory; AND

b) Patient has a history of at least six flares per year OR was hospitalized for a severe flare; AND

iii. The medication is prescribed by or in consultation with a rheumatologist, geneticist, nephrologist, oncologist, or hematologist.

B) Patient is Currently Receiving Ilaris. Approve for 1 year if the patient meets BOTH of the following (i and ii):

i. Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

ii. Patient meets at least one of the following (a or b):

a) When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include decreased frequency of attacks, resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, amyloid A), reduction in proteinuria, and/or stabilization of serum creatinine.

b) Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as decreased pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

Dosing:
Patient ≤ 40 kg: Start at 2 mg/kg every 4 weeks. The dose can be increased to 4 mg/kg every 4 weeks, if clinical response is not adequate. (2.3)
Patient > 40 kg: start at 150 mg every 4 weeks. The dose can be increased to 300mg every 4 weeks if clinical response is not adequate.

7. Gout, Acute Flare. Approve for 12 weeks if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND

B) Patient meets ONE of the following (i or ii):
- **i.** Patient meets ALL of the following (a, b, c, d, and e):
  - **a)** Patient has NOT received previous treatment with Ilaris for gout flare(s); AND
  - **b)** Patient has had ≥ 3 gout flares within the previous 12 months; AND
  - **c)** Patient has an intolerance, contraindication, or lack of response to nonsteroidal anti-inflammatory drugs (NSAIDs) for the treatment of acute gout flares; AND
  - **d)** Patient has an intolerance, contraindication, or lack of response to colchicine for the treatment of acute gout flares; AND
  - **e)** Patient is not a candidate for repeated courses of corticosteroids; OR
- **ii.** Patient meets ALL of the following (a, b, and c):
  - **a)** Patient has been previously treated with Ilaris for an acute gout flare resulting in a decrease or resolution of joint pain in the affected joints; AND
  - **b)** Patient requires retreatment for a new gout flare; AND
  - **c)** Patient has not received treatment with Ilaris in the previous 12 weeks; AND

C) According to the prescriber, patient is receiving or will be taking concomitant urate lowering medication for the prevention of gout unless contraindicated; AND
Note: Examples of uric acid lowering drugs include allopurinol, febuxostat, or probenecid.

D) Ilaris is prescribed by or in consultation with a rheumatologist.

Dosing:
Administer 150mg subcutaneously for 1 dose.
- Note: In patients who require re-treatment, there should be an interval of at least 12 weeks before receiving another dose.

Waste Management for All Indications.
Ilaris comes in a 6 mL, clear glass vial with flip off Cap/seal. It is preservation free, single use sterile vial

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Ilaris has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

1. **Concurrent Biologic Therapy.** Ilaris should not be administered in combination with another biologic agent for an inflammatory condition (see appendix A for examples) Ilaris has not been used in combination with TNF blocking agents. An increased incidence of serious infections has been associated with another IL-1 blocker, Kineret, when given in combination with TNF antagonists in patients with rheumatoid arthritis. Concomitant administration of Ilaris and other agents that block IL-1 or its receptors is not recommended.

2. **Rheumatoid Arthritis.** Ilaris has been studied for the treatment of rheumatoid arthritis. In a 12-week, Phase II, placebo-controlled, double-blind, dose-finding study, 277 patients who had failed treatment with MTX were randomized to Ilaris or placebo. The primary endpoint, the ACR 50 at Week 12, was statistically significantly higher

for Ilaris 150 mg SC every 4 weeks compared with placebo (26.5% vs. 11.4%, respectively; P = 0.028). There was not a statistically significant difference in ACR 50 for the other Ilaris treatment groups compared with placebo (Ilaris 300 mg SC every 2 weeks; Ilaris 600 mg loading dose followed by 300 mg SC every 2 weeks). Further studies are needed.

3. **COVID-19 (Coronavirus Disease 2019).** Forward all requests to the Medical Director. Note: This includes requests for cytokine release syndrome associated with COVID.

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

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12. Schlesinger N, Alten RE, Bardin T, et al. Canakinumab for acute gouty arthritis in patients with limited treatment options: results from two randomised, multicentre, active-controlled, double-blind trials and their initial extensions. Ann Rheum Dis. 2012 Nov;71(11):1839-48. doi: 10.1136/annrheumdis-2011-200908. Epub 2012 May 14.

HCPCS Code(s):	
J0638	Injection, canakinumab, 1 mg

APPENDIX A

Brand (generic name)	Mechanism of Action
Cimzia® (certolizumab pegol for SC injection)	Inhibition of TNF
Enbrel® (etanercept for SC injection)	Inhibition of TNF
Erelzi™ (etanercept-szzs for SC injection)	Inhibition of TNF
Humira® (adalimumab for SC injection)	Inhibition of TNF
Amjevita® (adalimumab-atto for SC injection)	Inhibition of TNF
Simponi® (golimumab for SC injection)	Inhibition of TNF
Simponi® Aria™ (golimumab for IV infusion)	Inhibition of TNF
Remicade® (infliximab for IV infusion)	Inhibition of TNF
Inflectra™ (infliximab-dyyb for IV infusion)	Inhibition of TNF
Renflexis® (infliximab-abda for IV infusion)	Inhibition of TNF
Actemra® (tocilizumab for IV infusion)	Inhibition of IL-6
Actemra® (tocilizumab for SC injection)	Inhibition of IL-6
Kevzara® (sarilumab for SC injection)	Inhibition of IL-6
Orencia® (abatacept for IV infusion)	T-cell costimulation modulator
Orencia® (abatacept for SC injection)	T-cell costimulation modulator
Rituxan® (rituximab for IV infusion)	CD20-directed cytolytic antibody
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1
Stelara® (ustekinumab for SC injection)	Inhibition of IL-12/23
Stelara® (ustekinumab for IV infusion)	Inhibition of IL-12/23
Siliq™ (brodalumab SC injection)	Inhibition of IL-17
Cosentyx™ (secukinumab for SC injection)	Inhibition of IL-17A
Taltz® (ixekizumab for SC injection)	Inhibition of IL-17A
Tremfya™ (guselkumab for SC injection)	Inhibition of IL-23
Otezla® (apremilast tablets)	Inhibition of PDE4
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1
Arcalyst® (rilonacept SC injection)	Inhibition of IL-1
Ilaris® (canakinumab SC injection)	Inhibition of IL-1

SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin;PDE4 – Phosphodiesterase 4; JAK – Janus kinase.