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PHARMACY POLICY STATEMENT
HAP CareSource™ Marketplace

DRUG NAME	Ilaris (canakinumab)
BENEFIT TYPE	Pharmacy
STATUS	Prior Authorization Required

Ilaris is an interleukin-1β blocker that was initially approved by the FDA in 2009. It is indicated for the treatment of certain autoinflammatory Periodic Fever Syndromes (CAPS, TRAPS, FMF, HIDS/MKD), Active Still's Disease (Adult-Onset Still's Disease [AOSD] and Systemic Juvenile Idiopathic Arthritis [SJIA]), and gout flares. Ilaris binds to IL-1β and neutralizes its activity by blocking its interaction with IL-1 receptors, but it does not bind IL-1α or IL-1 receptor antagonist (IL-1ra).
Cryopyrin-Associated Periodic Syndrome (CAPS) refer to rare genetic syndromes generally caused by mutations in the NLRP-3 gene (also known as CIAS1). The NLRP-3 gene encodes the protein cryopyrin, an important component of the inflammasome. Cryopyrin controls the activation of IL-1β. Mutations in NLRP-3 result in an overactive inflammasome resulting in excessive release of activated IL-1β that drives inflammation.
Still's disease is a severe autoinflammatory disease, driven by innate immunity by means of proinflammatory cytokines such as IL-1β. AOSD and SJIA are thought to represent a continuum of the same disease entity.

Ilaris (canakinumab) will be considered for coverage when the following criteria are met:

Adult-Onset Still's Disease (AOSD)

For **initial** authorization:
1. Member has a confirmed diagnosis of active AOSD supported by chart notes; AND
2. Medication must be prescribed by or in consultation with a rheumatologist; AND
3. Member has tried and failed a corticosteroid; AND
4. Member has moderate to severe disease, OR has tried and failed a conventional DMARD (e.g., methotrexate, cyclosporine); AND
5. Must have a negative tuberculosis test within the past 12 months.
6. **Dosage allowed/Quantity limit:** 4 mg/kg (up to max dose 300 mg) subcutaneously every 4 weeks. QL: 2 vials (2 mL) per 28 days

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes have been provided that show improvement of signs and symptoms of disease (i.e., systemic and articular manifestations, normalized CRP, reduced corticosteroid use).

If all the above requirements are met, the medication will be approved for an additional 12 months.

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Cryopyrin-Associated Periodic Syndrome (CAPS)

For **initial** authorization:

1. Member must be at least 4 years of age; AND
2. Medication must be prescribed by or in consultation with a rheumatologist or other physician experienced with periodic fever syndromes; AND
3. Member must be diagnosed with Familial Cold Autoinflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS); AND
4. Genetic testing results show gain-of-function mutation in the *NLRP3* gene; AND
5. Member has elevated inflammatory markers (e.g., serum amyloid A, C-reactive protein, erythrocyte sedimentation rate [SAA, CRP, ESR]); AND
6. Member displays symptoms of CAPS (e.g., rash, cold/stress-triggered episodes, hearing loss); AND
7. Must have a negative tuberculosis test within the past 12 months.
8. **Dosage allowed/Quantity limit:** 150 mg for body weight > 40 kg; 2 mg/kg for body weight between 15 kg and 40 kg. For children 15 kg to 40 kg with an inadequate response, the dose can be increased to 3 mg/kg. Administer subQ every 8 weeks.
   QL: 1 vial (1 mL) per 56 days

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes demonstrate positive clinical response including decreased inflammatory marker values and symptom improvement.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Familial Mediterranean Fever (FMF)

For **initial** authorization:

1. Medication is prescribed by or in consultation with a rheumatologist or other physician experienced with periodic fever syndromes; AND
2. Member has a diagnosis of familial Mediterranean fever; AND
3. Member is resistant to a compliant trial of colchicine at maximal appropriate dose (i.e., 1-3 mg/day) with ongoing disease activity reflected by:
   a) Recurrent clinical attacks (average 1 or more per month over a 3-month period) and/or
   b) Persistently elevated CRP or SAA between attacks; AND
4. Colchicine will be continued unless contraindicated or intolerable; AND
5. Must have a negative tuberculosis test within the past 12 months.
6. **Dosage allowed/Quantity limit:**
   Body weight ≤ 40 kg: starting dose is 2 mg/kg subQ every 4 weeks. The dose can be increased to 4 mg/kg every 4 weeks if the clinical response is not adequate.
   Body weight > 40 kg: starting dose is 150 mg subQ every 4 weeks. The dose can be increased to 300 mg every 4 weeks if the clinical response is not adequate.
   QL: 2 vials (2 mL) per 28 days

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes have been provided showing response to therapy such as reduced severity and/or frequency of flares, reduced SAA and/or CRP levels.

If all the above requirements are met, the medication will be approved for an additional 12 months.

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

For **initial** authorization:
1. Medication is prescribed by or in consultation with a rheumatologist or other physician experienced with periodic fever syndromes; AND
2. Member has a diagnosis of HIDS/MKD, confirmed by genetic testing results that show loss-of-function mutation in *MVK* gene; AND
3. Member has elevated inflammatory markers (e.g., serum levels of amyloid A, C-reactive protein, erythrocyte sedimentation rate [SAA, CRP, ESR]); AND
4. Member displays signs or symptoms of HIDS/MKD (e.g., GI symptoms, rash, fever attack triggered by vaccination, elevated urine mevalonate levels during disease flare); AND
5. Must have a negative tuberculosis test within the past 12 months.
6. **Dosage allowed/Quantity limit:**
   Body weight ≤ 40 kg: starting dose is 2 mg/kg subQ every 4 weeks. The dose can be increased to 4 mg/kg every 4 weeks if the clinical response is not adequate.
   Body weight > 40 kg: starting dose is 150 mg subQ every 4 weeks. The dose can be increased to 300 mg every 4 weeks if the clinical response is not adequate.
   QL: 2 vials (2 mL) per 28 days

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes have been provided showing response to therapy such as reduced severity and/or frequency of flares.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Systemic Juvenile Idiopathic Arthritis (SJIA)

For **initial** authorization:
1. Member must be 2 years of age or older and weigh ≥ 7.5 kg; AND
2. Medication must be prescribed by or in consultation with a rheumatologist; AND
3. Member must have active SJIA; AND
4. Member must have inadequate response to **ONE** of the following:
   a) Glucocorticoid;
   b) NSAID; AND
5. Member has had a negative tuberculosis test within the past 12 months.

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6. **Dosage allowed/Quantity limit**: 4 mg/kg subcutaneously every 4 weeks with a maximum dose of 300 mg. Quantity limit: 2 vials per 28 days.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
1. Chart notes have been provided that show the member has shown improvement of signs and symptoms of disease such as decreased joint swelling, decreased pain and improved quality of life.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)

For **initial** authorization:
1. Medication is prescribed by or in consultation with a rheumatologist or other physician experienced with periodic fever syndromes; AND
2. Member has a diagnosis of TRAPS, confirmed by genetic testing results that show gain-of-function mutation in *TNFRSF1A* gene; AND
3. Member has elevated inflammatory markers (e.g., serum levels of amyloid A, C-reactive protein, erythrocyte sedimentation rate [SAA, CRP, ESR]); AND
4. Member displays signs or symptoms of TRAPS (e.g., long-lasting fever episodes, abdominal pain, migratory rash, periorbital edema, myalgia, positive family history); AND
5. Must have a negative tuberculosis test within the past 12 months.
6. **Dosage allowed/Quantity limit:**
   Body weight ≤ 40 kg: starting dose is 2 mg/kg subQ every 4 weeks. The dose can be increased to 4 mg/kg every 4 weeks if the clinical response is not adequate.
   Body weight > 40 kg: starting dose is 150 mg subQ every 4 weeks. The dose can be increased to 300 mg every 4 weeks if the clinical response is not adequate.
   QL: 2 vials (2 mL) per 28 days

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes have been provided showing response to therapy such as reduced severity and/or frequency of flares.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Gout Flare

For **initial** authorization:
1. Member is at least 18 years of age; AND
2. Medication is prescribed by or in consultation with a rheumatologist; AND
3. Member has a diagnosis of gout with documentation of at least 3 flares in the past year; AND
4. Member has documentation of trial and failure of ALL 3 of the following:
   a) Non-steroidal anti-inflammatory drugs (NSAIDs)

b) Colchicine
c) Corticosteroids; AND

5. Member has a negative tuberculosis test within the past 12 months.
6. **Dosage allowed/Quantity limit:** 150 mg subQ. If retreatment is required, there must be an interval of at least 12 weeks before a new dose can be given.

If all the above requirements are met, the medication will be approved for 3 months.

For **reauthorization**:

1. Chart notes must show documentation of response to therapy such as reduced pain severity and/or fewer flares; AND
2. Member is experiencing a new flare; AND
3. Re-treatment is not occurring more frequently than every 12 weeks.

If all the above requirements are met, the medication will be approved for an additional 6 months.

HAP CareSource considers Ilaris (canakinumab) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
05/09/2017	New policy for Ilaris created. Policy SRx-0042 archived. For CAPS diagnosis: laboratory evidence requirement of a genetic mutation added. Diagnoses of TRAPS, HIDS/MKD and FMF were added. List of diagnoses considered not medically necessary added.
07/14/2017	Documentation of negative TB test was added to all diagnosis.
03/20/2019	TB test allowed to be done within 12 months prior to initiation of therapy; chest x-ray option removed.
09/29/2020	New diagnosis of Adult Onset Still's Disease added. Status corrected.
06/15/2021	At end of policy, replaced specific list of excluded diseases with general statement. CAPS: Updated references. Removed genetic test requirement (mutation not present in many patients), added biomarker and symptoms instead. Reduced initial approval duration from 12 months to 6 months, should see response much sooner. Specified renewal criteria. FMF: Updated references. Added specialist. Added diagnosis. Removed baseline PGA score. Removed CRP level. Removed minimum number of flares. Added trial of colchicine per guidelines. Specified renewal criteria. HIDS/MKD: Updated references. Added specialist. Added diagnosis. Removed baseline PGA score. Removed CRP level. Removed minimum number of flares. Reduced initial approval duration. Specified renewal criteria. TRAPS: Updated references. Added specialist. Added diagnosis. Removed baseline PGA score. Removed CRP level. Removed minimum number of flares. Reduced initial approval duration. Specified renewal criteria.
02/18/2022	Transferred to new template. AOSD: Added new reference. Changed wording of TB test requirement. Removed meet initial criteria from reauth section.
11/16/2023	Added new indication for gout flares.
06/21/2024	SJIA: added in consultation with for prescriber specialty; removed TB test and compliance with initial criteria from reauthorization criteria; added examples to

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	improvement of signs and symptoms in reauthorization criteria; simplified TB test wording; replaced 12 week trial of NSAID with just a trial of an NSAID per 2021 ACR guideline; removed methotrexate trial per 2021 ACR guideline; removed list of signs and symptoms for confirmation of diagnosis; added quantity limit; moved weight required from dosing to initial criteria. CAPS/TRAPS/MKD: Updated references, added new guideline ref (Romano 2022); added genetic testing requirements, edited symptom examples for CAPS, added symptomatology and inflammatory markers to TRAPS and MKD. FMF: Added reference. Changed “trial and failure” of colchicine to colchicine resistance, with definition (Lancieri 2023); added CRP and SAA to renewal. Added concomitant colchicine (Ozen 2016). AOSD: Updated references. Added specific renewal criteria (Colafrancesco 2019). Changed DMARD trial to only apply to mild disease instead of all, also removed duration and leflunomide (Vordenbaumen 2023). AOSD/CAPS/TRAPS/MKD/FMF: Added QL.

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