Clinical Policy: Canakinumab (Ilaris)
Reference Number: ERX.SPMN.09
Effective Date: 10/16
Last Review Date: 12/16

See Important Reminder at the end of this policy for important regulatory and legal information.

Policy/Criteria
It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that canakinumab (Ilaris®) is medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Cryopyrin-Associated Periodic Syndromes (must meet all):
      1. Prescribed by or in consultation with a rheumatologist or other physician experienced in the management of cryopyrin-associated periodic syndromes;
      2. Diagnosis of familial cold autoinflammatory syndrome (FCAS) or Muckle-Wells syndrome (MWS);
      3. Prescribed dose of Ilaris does not exceed 150 mg every 8 weeks.
   
      Approval duration: 12 weeks

   B. Systemic Juvenile Idiopathic Arthritis (must meet all):
      1. Prescribed by or in consultation with a rheumatologist;
      2. Diagnosis of systemic juvenile idiopathic arthritis (SJIA);
      3. Member has failed one of the following therapies unless contraindicated:
         a. A biologic for SJIA other than Ilaris;
         b. One or more non-steroidal anti-inflammatory drugs (NSAIDs) for ≥ 1 month and corticosteroids for ≥ 2 weeks;
         c. Methotrexate or leflunomide for ≥ 3 consecutive months;
      4. Prescribed dose of Ilaris does not exceed 300 mg every 4 weeks.

      Approval duration: 8 weeks

   C. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (must meet all):
      1. Prescribed by or in consultation with a rheumatologist or other physician experienced in the management of tumor necrosis factor receptor associated periodic syndrome (TRAPS);
      2. Diagnosis of TRAPS;
      3. Prescribed dose of Ilaris does not exceed 300 mg every 4 weeks.

      Approval duration: 8 weeks

   D. Hyperimmunoglobulin D Syndrome/Mevalonate Kinase Deficiency (must meet all):
      1. Prescribed by or in consultation with a rheumatologist or other physician experienced in the management of hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD);
2. Diagnosis of HIDS/MKD;
3. Prescribed dose of Ilaris does not exceed 300 mg every 4 weeks.

**Approval duration:** 8 weeks

E. **Familial Mediterranean Fever** (must meet all):
1. Prescribed by or in consultation with a rheumatologist or other physician experienced in the management of familial Mediterranean fever (FMF);
2. Diagnosis of FMF;
3. Member meets one of the following (a or b):
   a. Age < 4 years;
   b. Member has failed ≥ 6 months of colchicine at maximum indicated doses, unless intolerant or contraindicated;
4. Prescribed dose of Ilaris does not exceed 300 mg every 4 weeks.

**Approval duration:** 8 weeks

F. **Other diagnoses/indications:** Refer to ERX.SPMN.16 - Global Biopharm Policy.

II. **Continued Approval**
A. **All Indications** (must meet all):
   1. Currently receiving medication via health plan benefit or member has previously met all initial approval criteria;
   2. Member meets one of the following (a or b):
      a. Member is responding positively to therapy as evidenced by documentation of clinical response which may include:
         i. For FCAS, MWS, TRAPS, HIDS/MKD, and FMF: reduction/normalization of C-reactive protein (CRP) or serum amyloid A (SAA) levels; reduction of flare frequency, symptom severity, or duration;
         ii. For SJIA: quantitative measures such as physician global assessment of disease activity, parent or patient global assessment of wellbeing, number of joints with active arthritis, number of joints with limited range of motion, CRP, and functional ability (Childhood Health Assessment Questionnaire – [CHAQ]);
      b. Member has had an inadequate response to therapy, and request is for a dose increase;
   3. Prescribed regimen does not exceed the following:
      a. For FCAS and MWS: 150 mg every eight weeks;
      b. For SJIA, TRAPS, HIDS/MKD, and FMF: 300 mg every four weeks.

**Approval duration:** 12 months

B. **Other diagnoses/indications** (must meet 1 or 2):
   1. Currently receiving medication via health plan benefit and documentation supports positive response to therapy; or
Background

Description/Mechanism of Action:
Canakinumab is a human monoclonal anti-human IL-1β antibody of the IgG1/κ isotype. Ilaris binds to human 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 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 autoinflammatory disease, driven by innate immunity by means of pro-inflammatory cytokines such as interleukin 1β (IL-1β).

Formulations:
Ilaris is supplied in a sterile, single-use, colorless, 6 mL glass vial containing 150 of canakinumab as a white, preservative-free, lyophilized powder. Reconstitution with 1 mL of preservative-free sterile water for injection is required prior to administration.

FDA Approved Indications:
Ilaris is an interleukin-1β blocker/subcutaneous injectable formulation indicated for the treatment of:

- Periodic fever syndromes:
  - Cryopyrin-associated periodic syndromes (CAPS) in adults and children 4 years of age and older including:
    - Familial cold autoinflammatory syndrome (FCAS)
    - Muckle-Wells syndrome (MWS)
  - Tumor necrosis factor receptor associated periodic syndrome (TRAPS) in adult and pediatric patients
  - Hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD) in adult and pediatric patients
  - Familial Mediterranean fever (FMF) in adult and pediatric patients
- Active systemic juvenile idiopathic arthritis (SJIA) in patients aged 2 years and older

Appendices

Appendix A: Abbreviation Key
CAPS: cryopyrin-associated periodic syndromes
CHAQ: Childhood Health Assessment Questionnaire
CRP: C-reactive protein
Canakinumab

FCAS: familial cold autoinflammatory syndrome
FMF: familial Mediterranean fever
HIDS: hyperimmunoglobulin D syndrome
MKD: mevalonate kinase deficiency
MWS: Muckle-Wells syndrome
NSAID: non-steroidal anti-inflammatory drug
SAA: serum amyloid A
SJIA: active systemic juvenile idiopathic arthritis
TRAPS: tumor necrosis factor receptor associated periodic syndrome

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<td>J0638</td>
<td>Injection, canakinumab, 1 mg</td>
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Reviews, Revisions, and Approvals

Policy split from USS.SPMN.09 Cryopyrin-Associated Periodic Syndromes (CAPS) Treatments and Rheumatoid Arthritis and Ankylosing Spondylitis Treatments. Converted to new template. Removed all safety criteria. Added route of administration and dosing frequency per PI. Modified approval duration to 6 months for initial and 12 months for re-auth.
SJIA: removed question related to active systemic features; modified duration of treatment of NSAIDs and corticosteroids to for ≥ 1 month and ≥ 2 weeks, respectively per American College of Rheumatology recommendations; added methotrexate or leflunomide as an option for failure.

Added criteria for the new FDA-approved indications: TRAPS, HIDS/MKD, and FMF. Made the following changes to the existing criteria:
-CAPS: Modified specialist requirement to include physicians experienced in the management of CAPS. Removed age restriction as that is not an absolute contraindication. Added maximum dose criteria per package insert. Modified initial approval duration to 12 weeks (a single dose over 8 weeks + a 4 week buffer period).
-SJIA: Removed age restriction as that is not an absolute contraindication. Added maximum dose criteria per package insert. Modified initial approval duration to 8 weeks (a single dose over 4 weeks + a 4 week buffer period).
-Re-auth: Added examples of positive response for all indications. Added that continued therapy may be approved despite inadequate response if request is for a dose increase.
Canakinumab

Reviews, Revisions, and Approvals

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<td>Updated formulation section in background to 150 mg powder (vs 180 mg powder), and modified to be more concise. Updated references.</td>
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References


Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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