Clinical Policy: Canakinumab (Ilaris)

Reference Number: ERX.SPA.04
Effective Date: 04.01.17
Last Review Date: 11.17 Revision Log

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

Description
Canakinumab (Ilaris®) is an interleukin-1β blocker.

FDA Approved Indication(s)
Ilaris is 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

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Ilaris is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cryopryin-Associated Periodic Syndromes (must meet all)**:**
1. Diagnosis of FCAS or MWS;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 4 years;
4. Dose does not exceed 150 mg every 8 weeks.

Approval duration: 3 months

B. Tumor Necrosis Factor Receptor Associated Periodic Syndrome (must meet all)**:**
1. Diagnosis of TRAPS;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 2 years;
4. Dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

C. Hyperimmunoglobulin D Syndrome/Mevalonate Kinase Deficiency (must meet all)**:**
1. Diagnosis of HIDS/MKD;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 2 years;
4. Dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

D. Familial Mediterranean Fever (must meet all)**:**
1. Diagnosis of FMF,
2. Prescribed by or in consultation with a rheumatologist;

3. Age ≥ 2 years;
4. Member meets one of the following (a or b):
   a. Age < 4 years;
   b. Failure of a ≥ 6 month trial of colchicine at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

E. Systemic Juvenile Idiopathic Arthritis (must meet all)**:**
1. Diagnosis of sJIA;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 2 years;
4. Failure of one of the following therapies (a or b), unless all are contraindicated or clinically significant adverse effects are experienced:
   a. A corticosteroid for 2 weeks;
   b. Methotrexate or leflunomide for ≥ 3 consecutive months;
5. Dose does not exceed 300 mg every 4 weeks.

Approval duration: 6 months

F. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met 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. Documentation supports inadequate response to current dose, and request is for a dose increase;
2. If request is for a dose increase, new dose does not exceed:
   a. For FCAS and MWS: 150 mg every 8 weeks;
   b. For TRAPS, HIDS/MKD, FMF, and sJIA: 300 mg every 4 weeks.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CAPS: cryopyrin-associated periodic syndromes
CHAQ: Childhood Health Assessment Questionnaire
CRP: C-reactive protein
FCAS: familial cold autoinflammatory syndrome
FDA: Food and Drug Administration
FMF: familial Mediterranean fever
HIDS/MKD: hyperimmunoglobulin D syndrome/mevalonate kinase deficiency
MWS: Muckle-Wells syndrome
sJIA: systemic juvenile idiopathic arthritis
TRAPS: tumor necrosis factor receptor associated periodic syndrome

Appendix B: General Information

- Periodic fever syndromes are a group of rare autoinflammatory diseases that include cryopyrin-associated periodic syndromes (CAPS), tumor necrosis factor receptor associated periodic syndrome (TRAPS), hyperimmunoglobulin D syndrome (HIDS)/mevalonate kinase deficiency (MKD), and familial Mediterranean fever (FMF). Diagnosis of these diseases can be confirmed by genetic testing.
- Three related conditions make up the broader disease known as CAPS: familial cold auto-inflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal-onset multisystem inflammatory disease (NOMID), also known as chronic infantile neurologic cutaneous articular syndrome (CINCA). While Ilaris is FDA-approved for FCAS and MWS, it is not FDA-approved for use in patients with NOMID/CINCA.
- Ilaris is FDA-approved for TRAPS, HIDS/MKD, and FMF based on rapid and sustained disease control produced in a 16-week randomized control trial. Additional studies with Ilaris in these diseases are currently ongoing, including a 24-week randomized withdrawal period and a 72-week open-label treatment period. Ilaris is the first therapeutic option for TRAPS and HIDS/MKD and the first biologic option for FMF. In FMF, the current standard of care is colchicine, a relatively safe oral therapy indicated in patients ages 4 and up. Colchicine has well-established benefit in FMF and has been used for decades. Although no US clinical practice guidelines exist for TRAPS, HIDS/MKD, and FMF, the European League Against Rheumatism (EULAR) guidelines for the management of FMF recommend colchicine be initiated at diagnosis for all patients and response to therapy be assessed every 6 months.
- Pediatric American College of Rheumatology (ACR) responses are defined by achieving levels of percentage improvement (30%, 50%, and 70%) from baseline in at least 3 of the 6 core outcome variables, with worsening of greater than or equal to 30% in no more than one of the remaining variables. Core outcome variables included a 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, C-reactive protein (CRP), and functional ability (Childhood Health Assessment Questionnaire - CHAQ).
- Ilaris is an interleukin-1 blocker and has the potential to increase the risk of infection and reactivate latent, chronic infections. Healthcare providers should follow current CDC guidelines to evaluate and to treat possible latent tuberculosis infections before initiating therapy. Prior to initiation of therapy, it is highly recommended that all patients be immunized due to the increased risk of infection.
- Concomitant administration of Ilaris with TNF inhibitors (such as Enbrel®, Humira®, or Remicade®) and IL-1 blocking agents (such as Kineret®) is not recommended because this may increase the risk of serious infections.

Appendix C: Therapeutic Alternatives

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
colchicine (Colcrys™)	**Familial Mediterranean Fever** PO in 1-2 divided doses based on age: > 12 years: 1.2-2.4 mg/day 6-12 years: 0.9-1.8 mg/day 4-6 years: 0.3-1.8 mg/day	2.4 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CAPS (FCAS and MWS)	Weight > 40 kg: 150 mg SC every 8 weeks Weight ≥ 15 kg to ≤ 40 kg: 2 mg/kg SC every 8 weeks (if inadequate response, may increase to 3 mg/kg)	150 mg/8 weeks
TRAPS, HIDS/MKD, FMF	Weight ≤ 40 kg: 2 mg/kg SC every 4 weeks (if inadequate response, may increase to 4 mg/kg) Weight > 40 kg: 150 mg SC every 4 weeks (if inadequate response, may increase to 300 mg every 4 weeks)	300 mg/4 weeks
sJIA	Weight ≥ 7.5 kg: 4 mg/kg (up to a maximum of 300 mg) every 4 weeks	300 mg/4 weeks

VI. Product Availability

- Single-dose vial for reconstitution: 150 mg
- Single-dose vial: 150 mg/mL

VII. References

1. Ilaris Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals; December 2016. Available at www.ilaris.com. Accessed August 7, 2017.
2. Ringold S, Weiss PF, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis. Arthritis Care Res. 2013; 65(10): 2499-2512.
3. Beukelman T, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. Arthritis Care & Research, 2011; 63(4): 465-482.
4. 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.
5. Sag E, Bilginer Y, Ozen S. Autoinflammatory diseases with periodic fevers. Curr Rheumatol Rep. 2017; 19: 41.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	12.16	02.17
4Q17 Annual Review Converted to new template. All indications: Added age limits per FDA labeling. Except for SJIA, modified specialist requirement to remove physician experienced in the management of the relevant diagnosis since this is too general and not evaluable or enforceable. Changed initial approval durations from the duration of 1 dose + buffer time to the standard 6 months for all indications except CAPS (changed to 3 months). SJIA: Added requirement for trial of a corticosteroid, MTX, or leflunomide per SJIA guidelines.	09.12.17	11.17

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.