Clinical Policy: Canakinumab (Ilaris)

Reference Number: CP.PHAR.246
Effective Date: 08.01.16
Last Review Date: 05.20
Line of Business: Commercial, HIM, Medicaid

Revision Log

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

Description

Canakinumab (Ilaris®) is an interleukin-1 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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Ilaris is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Periodic Fever Syndromes (must meet all)**:**

1. Diagnosis of FCAS, MWS, TRAPS, HIDS/MKD, or FMF;
2. Prescribed by or in consultation with a rheumatologist;
3. Member meets one of the following (a or b):
   a. FCAS or MWS: age ≥ 4 years;
   b. TRAPS, HIDS/MKD, or FMF: age ≥ 2 years;
4. For FMF, 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 one of the following (a or b):
   a. FCAS or MWS (i or ii):

i. Weight 15 to 40 kg: 3 mg/kg/dose every 8 weeks;
ii. Weight > 40 kg: 150 mg every 8 weeks;

b. TRAPS, HIDS/MKD, or FMF (i or ii):
i. Weight ≤ 40 kg: 4 mg/kg/dose every 4 weeks;
ii. Weight > 40 kg: 300 mg every 4 weeks.

Approval duration:
Medicaid/HIM – 3 months for FCAS or MWS; 6 months for all other indications
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Systemic Juvenile Idiopathic Arthritis (must meet all)**:**

1. Diagnosis of SJIA;
2. Prescribed by or in consultation with a dermatologist, rheumatologist, or gastroenterologist;
3. Age ≥ 2 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) or leflunomide at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
   b. Failure of a ≥ 2-week trial of a systemic corticosteroid 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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy:
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
   a. FCAS or MWS (i or ii):
      i. Weight 15 to 40 kg: 3 mg/kg/dose every 8 weeks;
      ii. Weight > 40 kg: 150 mg every 8 weeks;
   b. TRAPS, HIDS/MKD, FMF, or SJIA (i or ii):
      i. Weight ≤ 40 kg: 4 mg/kg/dose every 4 weeks;
      ii. Weight > 40 kg: 300 mg every 4 weeks;
   c. SJIA: 300 mg every 4 weeks.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CAPS: Cryopyrin-Associated Periodic Syndromes
FCAS: Familial Cold Autoinflammatory Syndrome
FDA: Food and Drug Administration
FMF: Familial Mediterranean Fever
GI: gastrointestinal
HIDS: Hyperimmunoglobulin D Syndrome
MKD: Mevalonate Kinase Deficiency
MWS: Muckle-Wells Syndrome
SJIA: Systemic Juvenile Idiopathic Arthritis
TRAPS: Tumor Necrosis Factor Receptor Associated Periodic Syndrome

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
colchicine (Colcrys™)	**FMF** PO in 1-2 divided doses based on age: Age 4– 6 years: 0.3-1.8 mg/day Age 6 – 12 years: 0.9-1.8 mg/day Age > 12 years: 1.2-2.4 mg/day	2.4 mg/day
corticosteroids	**SJIA*** < 0.5 mg/kg/day PO of prednisone or equivalent	Varies
leflunomide (Arava®)	**SJIA***	10 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	100 mg PO QD for 2 days, then 10 mg QD or 100 mg PO QD for 1 day, then 10 mg EOD	
methotrexate (Rheumatrex®)	**SJIA** 0.5 – 1 mg/kg/week PO	30 mg/week

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.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): confirmed hypersensitivity to the active substance or to any of the excipients
- Boxed warning(s): none reported

Appendix D: 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 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 United States 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.
- Examples of positive response to therapy for periodic fever syndromes (FCAS, MWS, TRAPS, HIDS/MKD, and FMF) include reduction/normalization of: C-reactive protein (CRP) levels, serum amyloid A (SAA) levels, flare frequency, or severity and duration of symptoms (e.g., joint pain, rash, fever/chills, eye pain, fatigue).
- Examples of positive response to therapy for SJIA include improvement in: quantitative measures such as physician global assessment of disease activity, parent or patient global assessment of well-being, number of joints with active arthritis, number of joints with limited range of motion, CRP, and functional ability (CHAQ).
- Failure of a trial of conventional DMARDs:
    - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.

- Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.

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
CAPS (TRAPS, HIDS/MKD, FMF)	Weight > 40 kg: 150 mg SC every 4 weeks (if inadequate response, may increase to 300 mg every 4 weeks) Weight ≤ 40 kg: 2 mg/kg SC every 4 weeks (if inadequate response, may increase to 4 mg/kg)	300 mg/4 weeks
SJIA	Weight ≥ 7.5 kg: 4 mg/kg SC (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 Corporation; December 2016. Available at: www.ilaris.com. Accessed February 26, 2020.
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.
6. Foeldvari I, Wierk A. Effectiveness of leflunomide in patients with juvenile idiopathic arthritis in clinical practice. J Rheumatol. 2010; 37(8):1763.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.86.Arthritis Treatments and CP.PHAR.47.CAPS. FCAS, MWS: Removed criteria related to HBV, malignant disease, concomitant use with other biologics, and concurrent administration of live vaccines; added requirement related to dosing based on FDA approved dosing guidelines. SJIA: removed question related to active systemic features; modified duration of treatment of NSAIDs and corticosteroids to for ≥ 1 month and ≥ 2 weeks, respectively; added MTX or leflunomide as an option for failure. Re-auth: combined into All Indications; added criteria related to dosing reasons to discontinue. Modified approval duration to 6 months for initial and 12 months for renewal.	06.16	08.16
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. Added maximum dose criteria. Modified initial approval duration to 12 weeks. SJIA: Removed age restriction. Added maximum dose criteria per package insert. Modified initial approval duration to 8 weeks. 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. Updated formulation section in background to 150 mg powder (vs 180 mg powder), and modified to be more concise. Updated references.	11.16	12.16
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: Removed requirement for trial/failure of NSAID as it not a first line therapy recommended by the SJIA guidelines. Note: Safety criteria was applied according to the safety guidance discussed at CPAC. An exception was made to require TB screening for all patients prior to treatment to ensure that proper risk reduction measures are taking, though this is not specifically addressed in boxed warning.	08.17.17	11.17
2Q 2018 annual review: policies combined for Medicaid and Commercial lines of business; Commercial: split from CP.CPA.234; condensed all periodic fever syndromes into one criteria set; duration of initial approval for periodic fever syndromes modified to 6 months; added dermatologist and gastrointestinal specialist requirement to SJIA; removed requirement for TB testing from all criteria; moved examples of positive response to therapy to Appendix C: General	02.27.18	05.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Information; weight-based max dosing added for periodic fever syndromes diagnoses; references reviewed and updated.		
4Q 2018 annual review: no significant changes; references reviewed and updated.	09.04.18	11.18
2Q 2019 annual review: no significant changes; added HIM-Medical Benefit; references reviewed and updated.	02.26.19	05.19
2Q 2020 annual review: no significant changes; revised HIM-Meical Benefit line of business to HIM; references reviewed and updated.	02.28.20	05.20

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to

recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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