

## **Clinical Policy: Canakinumab (Ilaris)**

Reference Number: CP.PHAR.246

Effective Date: 08.01.16

Last Review Date: 05.21

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<sup>®</sup>) 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 Still's disease, including adult-onset Still's disease (AOSD) and 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<sup>®</sup> 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  $\geq$  4 years;
  - b. TRAPS, HIDS/MKD, or FMF: Age  $\geq$  2 years;
4. Documentation of one of the following (a – e):
  - a. For FCAS, classic signs and symptoms (e.g., recurrent, intermittent fever and rash often exacerbated by exposure to generalized cool ambient temperature) AND functional impairment limiting activities of daily living;

- b. For MWS, classic signs and symptoms (e.g., chronic fever and rash of waxing and waning intensity, sometimes exacerbated with exposure to generalized cool ambient temperature) AND functional impairment limiting activities of daily living;
- c. For TRAPS, chronic or recurrent disease activity with history of  $\geq 6$  flares within the last 12 months;
- d. For HIDS/MKD,  $\geq 3$  febrile acute flares within the last 6 months;
- e. For FMF, active disease with at least one flare per month and one of the following (i or ii):
  - i. Age  $< 4$  years;
  - ii. Failure of a  $\geq 6$ -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  $\leq 40$  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  $\geq 2$  years;
4. Member meets one of the following (a or b):
  - a. Failure of a  $\geq 3$  consecutive month trial of methotrexate (MTX) or leflunomide at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
  - b. Failure of a  $\geq 2$ -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. Adult-Onset Still’s Disease (must meet all):**

1. Diagnosis of AOSD;
2. Prescribed by or in consultation with a rheumatologist or hematologist;
3. Age  $\geq 18$  years;
4. Member meets one of the following (a or b):

- a. Failure of a  $\geq 3$  consecutive month trial of MTX, at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
  - b. Failure of a  $\geq 2$ -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

**D. 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, b, or c):
  - 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  $\leq 40$  kg: 4 mg/kg/dose every 4 weeks;
    - ii. Weight > 40 kg: 300 mg every 4 weeks;
  - c. SJIA or AOSD: 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.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
- B.** Combination use of biological disease-modifying antirheumatic drugs (bDMARDs), including any tumor necrosis factor (TNF) antagonists [Cimzia<sup>®</sup>, Enbrel<sup>®</sup>, Simponi<sup>®</sup>, Avsola<sup>™</sup>, Inflectra<sup>™</sup>, Remicade<sup>®</sup>, Renflexis<sup>™</sup>], interleukin agents [Arcalyst<sup>®</sup> (IL-1 blocker), Ilaris<sup>®</sup> (IL-1 blocker), Kineret<sup>®</sup> (IL-1RA), Actemra<sup>®</sup> (IL-6RA), Kevzara<sup>®</sup> (IL-6RA), Stelara<sup>®</sup> (IL-12/23 inhibitor), Cosentyx<sup>®</sup> (IL-17A inhibitor), Taltz<sup>®</sup> (IL-17A inhibitor), Siliq<sup>™</sup> (IL-17RA), Ilumya<sup>™</sup> (IL-23 inhibitor), Skyrizi<sup>™</sup> (IL-23 inhibitor), Tremfya<sup>®</sup> (IL-23 inhibitor)], janus kinase inhibitors (JAKi) [Xeljanz<sup>®</sup>/Xeljanz<sup>®</sup> XR, Rinvoq<sup>™</sup>], anti-CD20 monoclonal antibodies [Rituxan<sup>®</sup>, Riabni<sup>™</sup>, Ruxience<sup>™</sup>, Truxima<sup>®</sup>, and Rituxan Hycela<sup>®</sup>], selective co-stimulation modulators [Orencia<sup>®</sup>], or integrin receptor antagonists [Entyvio<sup>®</sup>] because of the possibility of increased immunosuppression, neutropenia and increased risk of infection.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

AOSD: adult-onset Still’s disease

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

MTX: methotrexate

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.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
colchicine (Colcris <sup>™</sup> )	<b>FMF</b> 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 (e.g., prednisone, methylprednisolone)	<b>SJIA*</b> < 0.5 mg/kg/day PO of prednisone or equivalent <b>AOSD*</b> Varies	Varies
leflunomide (Arava <sup>®</sup> )	<b>SJIA*</b>	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 <sup>®</sup> )	<b>SJIA</b> 0.5 – 1 mg/kg/week PO <b>AOSD*</b> 7.5 – 25 mg/week PO	30 mg/week

*Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) 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:
  - 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).
  - 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).
  - AOSD include normalization or improvement in laboratory test results for serum markers of inflammation (e.g., ESR or CRP), sustained improvement in member's

- symptoms and disease stability. Chart notes indicating improvement in rash, joint pain and/or swelling and fevers.
- 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, AOSD	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 injection, lyophilized powder for reconstitution: 150 mg
- Single-dose vial for injection, solution: 150 mg/mL

## VII. References

1. Ilaris Prescribing Information. East Hanover, NJ; Novartis Pharmaceuticals Corporation; September 2020. Available at: [www.ilaris.com](http://www.ilaris.com). Accessed January 11, 2021.
2. Foeldvari I, Wierk A. Effectiveness of leflunomide in patients with juvenile idiopathic arthritis in clinical practice. *J Rheumatol*. 2010; 37(8):1763.
3. Franchini S, Dagna L, Salvo F, et al. Efficacy of Traditional and Biologic Agents in Different Clinical Phenotypes of Adult-Onset Still's Disease. *Arthritis Rheum*. 2010;62(8):2530-2535.
4. 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.

5. 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.
6. Jamilloux Y, Gerfaut-Valentin M, Henry T, et al. Treatment of adult-onset Still's disease: a review. *Ther Clin Risk Manag.* 2014;11:33-43.
7. 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.
8. Sag E, Bilginer Y, Ozen S. Autoinflammatory diseases with periodic fevers. *Curr Rheumatol Rep.* 2017; 19: 41.

**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.

HCPCS Codes	Description
J0638	Injection, canakinumab, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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 Information; weight-based max dosing added for periodic fever syndromes diagnoses; references reviewed and updated.	02.27.18	05.18
4Q 2018 annual review: no significant changes; references reviewed and updated.	09.04.18	11.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
Criteria added for new FDA approved indication: AOSD; added HCPCS code; updated Appendix B; references reviewed and updated.	10.20.20	11.20
2Q 2021 annual review: added requirements to confirm diagnosis/severity for periodic fever syndromes; added combination of bDMARDs under Section III; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.23.21	05.21

**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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