RXADVANCE
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Clinical Policy Title:	canakinumab
Policy Number:	RxA.164
Drug(s) Applied:	Ilaris®
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

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

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Canakinumab (Ilaris®)	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
	Still's Disease (SJIA and AOSD)	Weight ≥ 7.5 kg: 4 mg/kg SC (up to a maximum of 300 mg) every 4 weeks	300 mg/4 weeks

Dosage Forms

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

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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

Commercial: 6 months

Medicaid: 3 months for FCAS or MWS; 6 months for all other indications

B. Still's Disease (must meet all)**:**

1. Diagnosis of SJIA or AOSD;
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

Commercial: 6 months

Medicaid: 6 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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 ≤ 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
Commercial: 6 months
Medicaid: 12 months

III. Appendices

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
AOSD: Adult-Onset Still's Disease
MTX: Methotrexate

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*** 100 mg PO once daily for 2 days, then 10 mg once daily or 100 mg PO once daily for 1 day,	10 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	then 10 mg EOD	
methotrexate (Rheumatrex®)	**SJIA** 0.5 – 1 mg/kg 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.

References

1. Ilaris Prescribing Information. East Hanover, NJ; Novartis Pharmaceuticals Corporation; June 2020. Available at: www.ilaris.com. Accessed July 8, 2020.
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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.
7. Jahan A, Dewan V, Yadav TP. Leflunomide in systemic onset juvenile idiopathic arthritis. Indian Pediatr. 2012;49(9).

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated. 2. Line of Business Policy Applies to was updated to all lines of business. 3. Background was updated to include new indication, AOSD information. 4. Dosing information was updated to include new indication AOSD. 5. Continued therapy criteria II.A.1 was rephrased to “Currently receiving medication that has been authorized by RxAdvance…”. 6. Appendix A was updated: added AOSD & MTX. 7. References were updated.	7/8/2020	09/14/2020