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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: | 09/14/2021 |
| 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 |

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

Dosage Forms

- 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. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. For FMF, member meets one of the following (a or b):
 - a. Age $<$ 4 years;
 - b. 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

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 \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 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

Commercial: 6 months

Medicaid: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has 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

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

| 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 | 10 mg/day |

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|--------------|---|-----------------------------|
| | daily or 100 mg PO once daily for 1 day, then 10 mg EOD | |
| methotrexate | SJIA 0.5 – 1 mg/kg PO | 30 mg/week |

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

*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.

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; September 2020. Available at: www.ilaris.com. Accessed February 19, 2021.
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. Accessed February 19, 2021.
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. Accessed February 19, 2021.
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. Accessed February 19, 2021.
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. Accessed February 19, 2021.
7. Jahan A, Dewan V, Yadav TP. Leflunomide in systemic onset juvenile idiopathic arthritis. Indian Pediatr. 2012;49(9). Accessed February 19, 2021.

| Review/Revision History | Review/Revised Date | P&T Approval Date |
|--|---------------------|-------------------|
| Policy established. | 01/2020 | 02/07/2020 |
| Policy was reviewed: <ol style="list-style-type: none"> 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 |
| Policy was reviewed: <ol style="list-style-type: none"> 1. Dosage form updated. 2. Updated Appendix B: Removed brand Rheumatrex as it was discontinued. 3. Statement about drug listing format in Appendix B is rephrased to | 02/19/2021 | 09/14/2021 |

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| <p>"Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only".</p> <p>4. References were reviewed and updated.</p> | | |