CareSource Rxinnovations

PHARMACY POLICY STATEMENT
Marketplace

DRUG NAME	Ilaris (canakinumab)
BILLING CODE	Must use valid NDC
BENEFIT TYPE	Pharmacy
SITE OF SERVICE ALLOWED	Home/Office/Outpatient
STATUS	Prior Authorization Required

Ilaris is an interleukin-1β blocker that was initially approved by the FDA in 2009. It is indicated for the treatment of certain autoinflammatory Periodic Fever Syndromes, and for Still's Disease (Adult-Onset Still's Disease [AOSD] and Systemic Juvenile Idiopathic Arthritis [SJIA]). Ilaris binds to IL-1β and neutralizes its activity by blocking its interaction with IL-1 receptors, but it does not bind IL-1α or IL-1 receptor antagonist (IL-1ra).

CAPS refer to rare genetic syndromes generally caused by mutations in the NLRP-3 gene (also known as CIAS1). The NLRP-3 gene encodes the protein cryopyrin, an important component of the inflammasome. Cryopyrin controls the activation of IL-1β. Mutations in NLRP-3 result in an overactive inflammasome resulting in excessive release of activated IL-1β that drives inflammation. Still's disease is a severe autoinflammatory disease, driven by innate immunity by means of proinflammatory cytokines such as IL-1β. AOSD and SJIA are thought to represent a continuum of the same disease entity.

Ilaris (canakinumab) will be considered for coverage when the following criteria are met:

Adult-Onset Still's Disease (AOSD)

For **initial** authorization:

1. Member must have a confirmed diagnosis of active Adult-Onset Still's Disease supported by chart notes; AND
2. Medication must be prescribed by or in consultation with a rheumatologist; AND
3. Must have a negative tuberculosis test within the past 12 months; AND
4. Member has tried and failed, or unable to tolerate **both** of the following (taken together or separately):
   a) A trial of a corticosteroid (prednisone or methylprednisolone)
   b) A 2-month trial of a conventional DMARD (e.g., methotrexate, cyclosporine, leflunomide, etc.).
5. **Dosage allowed/Quantity limit:** 4 mg/kg (up to max dose 300 mg) subcutaneously every 4 weeks.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes have been provided that show the member has shown improvement of signs and symptoms of disease.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Cryopyrin-Associated Periodic Syndrome (CAPS)

For **initial** authorization:

1. Member must be 4 years of age or older; AND

2. Medication must be prescribed by or in consultation with a rheumatologist or other specialist familiar with periodic fever syndromes; AND
3. Member must be diagnosed with Familial Cold Autoinflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS); AND
4. Member has elevated inflammatory markers (e.g., serum levels of amyloid A, C-reactive protein, erythrocyte sedimentation rate); AND
5. Member displays symptoms of CAPS (e.g., skin rash, musculoskeletal pain, central nervous system manifestations, hearing loss, conjunctivitis, cold/stress-triggered flares); AND
6. Must have a negative tuberculosis test within the past 12 months.
7. **Dosage allowed/Quantity limit:** 150 mg for body weight > 40 kg; 2 mg/kg for body weight between 15 kg and 40 kg. For children 15 kg to 40 kg with an inadequate response, the dose can be increased to 3 mg/kg. Administer subQ every 8 weeks.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes demonstrate positive clinical response including decreased inflammatory marker values and symptom improvement.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Familial Mediterranean Fever (FMF)

For **initial** authorization:
1. Medication is prescribed by or in consultation with a rheumatologist or other physician experienced with periodic fever syndromes; AND
2. Member has a diagnosis of familial Mediterranean fever; AND
3. Member has had a compliant trial and failure of colchicine at maximal appropriate dose for at least 6 months unless contraindicated or intolerable; AND
4. Must have a negative tuberculosis test within the past 12 months.
5. **Dosage allowed/Quantity limit:** Body weight ≤ 40 kg: starting dose is 2 mg/kg every 4 weeks. The dose can be increased to 4 mg/kg every 4 weeks if the clinical response is not adequate. Body weight > 40 kg: starting dose is 150 mg every 4 weeks. The dose can be increased to 300 mg every 4 weeks if the clinical response is not adequate.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes have been provided showing response to therapy such as reduced severity and/or frequency of flares.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)

For **initial** authorization:
1. Medication is prescribed by or in consultation with a rheumatologist or other physician experienced with periodic fever syndromes; AND
2. Member has a diagnosis of HIDS/MKD; AND
3. Must have a negative tuberculosis test within the past 12 months.

4. **Dosage allowed/Quantity limit:** Body weight ≤ 40 kg: starting dose is 2 mg/kg every 4 weeks. The dose can be increased to 4 mg/kg every 4 weeks if the clinical response is not adequate. Body weight > 40 kg: starting dose is 150 mg every 4 weeks. The dose can be increased to 300 mg every 4 weeks if the clinical response is not adequate.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:
1. Chart notes have been provided showing response to therapy such as reduced severity and/or frequency of flares.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Systemic Juvenile Idiopathic Arthritis (SJIA)

For **initial** authorization:
1. Member must be 2 years of age or older; AND
2. Member must have a documented negative TB test (i.e., tuberculosis skin test (PPD), an interferon-release assay (IGRA)) within 12 months prior to starting therapy; AND
3. Medication must be prescribed by a rheumatologist; AND
4. Member must have active systemic juvenile idiopathic arthritis, as indicated by arthritis involving two or more joints AND **one** or more of the following:
   a) Evanescent erythematous rash;
   b) Fever for at least two weeks
   c) Generalized lymphadenopathy;
   d) Hepatomegaly or splenomegaly;
   e) Pericarditis, pleuritis, or peritonitis; AND
5. Member must have inadequate response to ALL of the following:
   a) Glucocorticoid injection;
   b) Methotrexate;
   c) NSAIDs after a 12-week trial.
      6. **Dosage allowed/Quantity limit:** 4 mg/kg (with a maximum of 300 mg) for members with a body weight ≥ 7.5 kg. Administer subcutaneously every 4 weeks.

If all the above requirements are met, the medication will be approved for 12 months.

For **reauthorization**:
1. Must have been retested for TB with a negative result within the past 12 months; AND
2. Member must be in compliance with all other initial criteria; AND
3. Chart notes have been provided that show the member has shown improvement of signs and symptoms of disease.

If all the above requirements are met, the medication will be approved for an additional 12 months.

Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS)

For **initial** authorization:
1. Medication is prescribed by or in consultation with a rheumatologist or other physician experienced with periodic fever syndromes; AND
2. Member has a diagnosis of TRAPS; AND
3. Must have a negative tuberculosis test within the past 12 months.
4. **Dosage allowed/Quantity limit:** Body weight ≤ 40 kg: starting dose is 2 mg/kg every 4 weeks. The dose can be increased to 4 mg/kg every 4 weeks if the clinical response is not adequate. Body weight

> 40 kg: starting dose is 150 mg every 4 weeks. The dose can be increased to 300 mg every 4 weeks if the clinical response is not adequate.

If all the above requirements are met, the medication will be approved for 6 months.

For **reauthorization**:

1. Chart notes have been provided showing response to therapy such as reduced severity and/or frequency of flares.

If all the above requirements are met, the medication will be approved for an additional 12 months.

CareSource considers Ilaris (canakinumab) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
05/09/2017	New policy for Ilaris created. Policy SRx-0042 archived. For CAPS diagnosis: laboratory evidence requirement of a genetic mutation added. Diagnoses of TRAPS, HIDS/MKD and FMF were added. List of diagnoses considered not medically necessary added.
07/14/2017	Documentation of negative TB test was added to all diagnosis.
03/20/2019	TB test allowed to be done within 12 months prior to initiation of therapy; chest x-ray option removed.
09/29/2020	New diagnosis of Adult Onset Still's Disease added. Status corrected.
06/15/2021	At end of policy, replaced specific list of excluded diseases with general statement. CAPS: Updated references. Removed genetic test requirement (mutation not present in many patients), added biomarker and symptoms instead. Reduced initial approval duration from 12 months to 6 months, should see response much sooner. Specified renewal criteria. FMF: Updated references. Added specialist. Added diagnosis. Removed baseline PGA score. Removed CRP level. Removed minimum number of flares. Added trial of colchicine per guidelines. Specified renewal criteria. HIDS/MKD: Updated references. Added specialist. Added diagnosis. Removed baseline PGA score. Removed CRP level. Removed minimum number of flares. Reduced initial approval duration. Specified renewal criteria. TRAPS: Updated references. Added specialist. Added diagnosis. Removed baseline PGA score. Removed CRP level. Removed minimum number of flares. Reduced initial approval duration. Specified renewal criteria.
02/18/2022	Transferred to new template. AOSD: Added new reference. Changed wording of TB test requirement. Removed meet initial criteria from reauth section.

References:

1. Ilaris [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; September 2020
2. Shinkai K, McCalmont TH, Leslie KS. Cryopyrin-associated periodic syndromes and autoinflammation. Clin Exp Dermatol. 2008;33(1):1-9.
3. Lachmann HJ, Kone-Paut I, Kuemmerle-Deschner JB, et al; Canakinumab in CAPS Study Group. Use of canakinumab in the cryopyrin-associated periodic syndrome. N Engl J Med. 2009;360(23):2416-2425.
4. American College of Rheumatology. Guidelines for the management of rheumatoid arthritis: American College of Rheumatology Ad Hoc Committee on Clinical Guidelines. Arthritis Rheuma. 1996;39(5):713-723.

5. Jamilloux Y, Gerfaud-Valentin M, Henry T, Sève P. Treatment of adult-onset Still's disease: a review. *Ther Clin Risk Manag*. 2014;11:33-43. Published 2014 Dec 22.
6. Govoni M, Bortoluzzi A, Rossi D, Modena V. How I treat patients with adult onset Still's disease in clinical practice. *Autoimmun Rev*. 2017;16(10):1016-1023.
7. Kedor C, Listing J, Zernicke J, et al. Canakinumab for Treatment of Adult-Onset Still's Disease to Achieve Reduction of Arthritic Manifestation (CONSIDER): phase II, randomised, double-blind, placebo-controlled, multicentre, investigator-initiated trial. Annals of the Rheumatic Diseases. Published Online First: 13 May 2020.
8. Yamaguchi M, et al. Diagnostic criteria for adult onset Still's disease (AOSD). J Rheumatol. 19:424-30, 1992.
9. Galozzi P, Baggio C, Bindoli S, et al. Development and Role in Therapy of Canakinumab in Adult-Onset Still's Disease. Front Pharmacol. 2018;9:1074. Published 2018 Sep 21. doi:10.3389/fphar.2018.01074.
10. Cavalli G, Tomelleri A, De Luca G, et al. Efficacy of canakinumab as first-line biologic agent in adult-onset Still's disease. Arthritis Res Ther 21, 54 (2019).
11. Junge G, Mason J, Feist E. Adult onset Still's disease – The evidence that anti-interleukin-1 treatment is effective and well-tolerated (a comprehensive literature review). Semin Arthritis Rheum. 2017;47(2):295-302.
12. Aarntzen EHJG, van Riel PLCM, Barrera P. Refractory adult onset Still's disease and hypersensitivity to non-steroidal anti-inflammatory drugs and cyclo-oxygenase-2 inhibitors: are biological agents the solution?. *Annals of the Rheumatic Diseases* 2005;64:1523-1524.
13. Efthimiou P. Adult Onset Still's Disease. NORD (National Organization for Rare Disorders). https://rarediseases.org/rare-diseases/adult-onset-stills-disease/. Published 2015. Accessed September 29, 2020.
14. Mandl LA, O'Dell JR, Romain PL. Treatment of adult Still's disease. In: Post TW, ed. UpToDate. Waltham, MA: UpToDate Inc.
15. DeWitt EM, Kimura Y, Beukelman T, et al. Consensus treatment plans for new-onset systemic juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)*. 2012;64(7):1001-1010.
16. Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis. Recommendations for the Medical Therapy of Children With Systemic Juvenile Idiopathic Arthritis and Tuberculosis Screening Among Children Receiving Biologic Medications Vol. 65, No. 10, October 2013, pp 2499–2512.
17. Ferrara G, Mastrangelo G, Barone P, et al. Methotrexate in juvenile idiopathic arthritis: advice and recommendations from the MARAJIA expert consensus meeting. *Pediatr Rheumatol Online J*. 2018;16(1):46. Published 2018 Jul 11.
18. Welzel T, Kuemmerle-Deschner JB. Diagnosis and Management of the Cryopyrin-Associated Periodic Syndromes (CAPS): What Do We Know Today?. *J Clin Med*. 2021;10(1):128. Published 2021 Jan 1. doi:10.3390/jcm10010128
19. De Benedetti F, Gattorno M, Anton J, et al. Canakinumab for the Treatment of Autoinflammatory Recurrent Fever Syndromes. *N Engl J Med*. 2018;378(20):1908-1919. doi:10.1056/NEJMoa1706314
20. 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. doi:10.1136/annrheumdis-2015-208690
21. Efthimiou P, Kontzias A, Hur P, Rodha K, Ramakrishna GS, Nakasato P. Adult-onset Still's disease in focus: Clinical manifestations, diagnosis, treatment, and unmet needs in the era of targeted therapies. *Semin Arthritis Rheum*. 2021;51(4):858-874. doi:10.1016/j.semarthrit.2021.06.004

Effective date: 07/01/2022
Revised date: 02/18/2022