

Ilaris® (canakinumab)

When requesting Ilaris® (canakinumab), the individual requiring treatment must be diagnosed with an FDA-approved indication and meet the specific coverage guidelines and applicable safety criteria for the covered indication.

FDA-Approved Indications

Ilaris is indicated for the treatment of 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)

Ilaris is indicated for the treatment of Tumor Necrosis Factor (TNF) receptor Associated Periodic Syndrome (TRAPS) in adults and pediatric patients.

Ilaris is indicated for the treatment of Hyperimmunoglobulin D (Hyper-IgD) Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD) in adult and pediatric patients.

Ilaris is indicated for the treatment of Familial Mediterranean Fever (FMF) in adult and pediatric patients.

Ilaris is indicated for the treatment of active systemic Juvenile Idiopathic Arthritis (sJIA) in patients aged 2 years and older.

Coverage Guidelines

For an initial authorization (all indications):

Cryopyrin-Associated Periodic Syndromes (CAPS):

- An individual is 4 years of age or older **AND**
- Ilaris is prescribed by or in consultation with one of the following specialist: rheumatologist, geneticist, allergist/immunologist, or dermatologist

Familial Mediterranean Fever (FMF):

- Ilaris is prescribed by or in consultation with one of the following specialists: rheumatologist, nephrologist, geneticist, gastroenterologist, oncologist, or hematologist

**Hyperimmunoglobulin D syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)
OR Tumor Necrosis Factor Receptor Associated Periodic Syndrome (TRAPS):**

- Ilaris is prescribed by or in consultation with one of the following specialists: rheumatologist, nephrologist, geneticist, oncologist, or hematologist

Systemic Juvenile Idiopathic Arthritis (sJIA):

- An individual is 2 years of age or older **AND**

- Ilaris is prescribed by or in consultation with a rheumatologist **AND**
- Has tried at least 2 other biologic agents (e.g., tocilizumab, Kineret, abatacept, etanercept, adalimumab, infliximab) **OR**
- Has features of poor prognosis (e.g., arthritis of the hip, radiographic damage, active systemic disease such as fever, elevated inflammatory markers) and has tried Actemra or Kineret **OR**
- Has active systemic features with concerns of progression to macrophage activation syndrome (MAS) and has tried Kineret

For re-authorization (all indications):

- An individual is responding to Ilaris therapy

Approval duration (initial): 3 months (*applies to CAPS and sJIA*)

Approval duration (initial): 4 months (*applies to FMF, TRAPS, and HIDS/MKD*)

Approval duration (renewal): 12 months

Dosing Recommendations

Cryopyrin-Associated Periodic Syndromes (CAPS):

The recommended dose is 150 mg for patients with body weight greater than 40 kg and 2 mg/kg for patients with body weight 15 to 40 kg administered subcutaneously every 8 weeks. The dose can be increased to 3 mg/kg in patients 15 to 40 kg with an inadequate response.

Tumor Necrosis Factor (TNF) receptor Associated Periodic Syndrome (TRAPS)/ Hyperimmunoglobulin D (Hyper-IgD) Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)/ Familial Mediterranean Fever (FMF)

For body weight less than or equal to 40 kg: The recommended 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

For body weight greater than 40 kg: The recommended 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.

Systemic Juvenile Idiopathic Arthritis:

The recommended dose is 4 mg/kg, with a maximum of 300 mg, for patients with a body weight greater than or equal to 7.5 kg every 4 weeks.

References

1. Ilaris® for subcutaneous injection [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; December 2016.
2. Hoffman HM, Throne ML, Amar NJ, et al. Efficacy and safety of rilonacept (interleukin-1 Trap) in patients with cryopyrin-associated periodic syndromes: results from two sequential placebo-controlled studies. *Arthritis Rheum.* 2008;58:2443-2452.

3. Shinkai K, McCalmont TH, Leslie KS. Cryopyrin-associated periodic syndromes and autoinflammation. *Clin Exp Dermatol*. 2008;33:1-9.
4. 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. *Arthritis Rheum*. 2013;65(10):2499-2512.
5. Ozen S, Hoffman HM, Frenkel J, et al. Familial Mediterranean Fever (FMF) and beyond: a new horizon. Fourth International Congress on the Systemic Autoinflammatory Diseases held in Bethesda, USA, 6-10 November 2005. *Ann Rheum Dis*. 2006;65(7):961-964.
6. 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;360:2416-2425.
7. Russo RA, Melo-Gomes S, Lachmann HJ, et al. Efficacy and safety of canakinumab therapy in paediatric patients with cryopyrin-associated periodic syndrome: a single-centre, real-world experience. *Rheumatology (Oxford)*. 2014;53(4):665-670.
8. Kuemmerle-Deschner JB, Hachulla E, Cartwright R, et al. Two-year results from an open-label, multicentre, phase III study evaluating the safety and efficacy of canakinumab in patients with cryopyrin-associated periodic syndrome across different severity phenotypes. *Ann Rheum Dis*. 2011;70(12):2095-2102.
9. Sibley CH, Chioato A, Felix S, et al. A 24-month open-label study of canakinumab in neonatal-onset multisystem inflammatory disease. *Ann Rheum Dis*. 2015;74(9):1714-1719.
10. Kuemmerle-Deschner JB, Ramos E, Blank N, et al. Canakinumab (ACZ885, a fully human IgG1 anti-IL-1 β mAb) induces sustained remission in pediatric patients with cryopyrin-associated periodic syndrome (CAPS). *Arthritis Res Ther*. 2011;13(1):R34.
11. Genetics Home Reference. US National Library of Medicine. Available at: <https://ghr.nlm.nih.gov/>. Accessed on October 29, 2018. Search terms: TRAPS, familial Mediterranean fever, MKD.
12. 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.
13. ter Haar NM, Oswald M, Jeyaratnam J, et al. Recommendations for the management of autoinflammatory diseases. *Ann Rheum Dis*. 2015;74(9):1636-1644.
14. Kimura Y, Morgan DeWitt E, Beukelman T, et al. Adding Canakinumab to the Childhood Arthritis and Rheumatology Research Alliance Consensus Treatment Plans for Systemic Juvenile Idiopathic Arthritis: comment on the article by DeWitt et al. *Arthritis Care Res (Hoboken)*. 2014;66(9):1430-1431.
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. Ruperto N, Brunner HI, Quartier P, et al. Two randomized trials of canakinumab in systemic juvenile idiopathic arthritis. *N Engl J Med*. 2012;367(25):2396-2406.
17. Novartis. Efficacy, safety and tolerability of ACZ885 in patients with active rheumatoid arthritis. In; ClinicalTrials.gov [Internet]. Bethesda (MD): National Library of Medicine (US). Accessed on October 29, 2018. Available from: <http://www.clinicaltrials.gov/ct2/show/NCT00424346?term=acz885&rank=10>. NLM Identifier: NCT00424346
18. Alten R, Gomez-Reino J, Durez P, et al. Efficacy and safety of the human anti-IL-1 β monoclonal antibody canakinumab in rheumatoid arthritis: results of a 12-week, Phase II, dose-finding study. *BMC Musculoskelet Disord*. 2011;12:153.
19. Kitley JL, Lachmann HJ, Pinto A, et al. Neurologic manifestations of the cryopyrin-associated periodic syndrome. *Neurology*. 2010;74(16):1267-1270.
20. Ruperto N, Quartier P, Wulfraat N, et al. A phase II, multicenter, open-label study evaluating dosing and preliminary safety and efficacy of canakinumab in systemic juvenile idiopathic arthritis with active systemic features. *Arthritis Rheum*. 2012;64(2):557-567.
21. Rissanen A, Howard CP, Botha J, et al. Effect of anti-IL-1 β antibody (canakinumab) on insulin secretion rates in impaired glucose tolerance or type 2 diabetes: results of a randomized, placebo-controlled trial. *Diabetes Obes Metab*. 2012;14(12):1088-1096.
22. Moran A, Bundy B, Becker DJ, et al. Interleukin-1 antagonism in type 1 diabetes of recent onset: two multicentre, randomised, double-blind, placebo-controlled trials. *Lancet*. 2013;381(9881):1905-1915.

23. Sivera F, Wechalekar MD, Andrés M, et al. Interleukin-1 inhibitors for acute gout. *Cochrane Database Syst Rev*. 2014 Sep 1;9:CD009993.
24. Koné-Paut I, Galeotti C. Current treatment recommendations and considerations for cryopyrin-associated periodic syndrome. *Expert Rev Clin Immunol*. 2015;11(10):1083-1092.