Cytokine and CAM Antagonists: CAPs Agents Utilization Management Criteria

Therapeutic Class:	Cytokine and CAM Antagonists: CAPs Agents
Non-Preferred Agents:	Kineret (anakinra), Ilaris (canakinumab), Arcalyst (rilonacept)
Preferred Agents:	None
Implementation Date:	1/1/2026
Prepared For:	CT Medicaid
PDL Status:	Non-preferred Agents
Background:	Cryopyrin-associated periodic syndrome (CAPS) is a group of autoinflammatory conditions that vary in severity. These conditions from least to most severe include familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and neonatal multisystem inflammatory disease (NOMID) also known as chronic infantile neurological cutaneous and articular syndrome (CINCA). Genetic mutations encoding cryopyrin cause an increased production of interleukin-1β leading to proinflammatory consequences. The CAPS agents include anakinra, canakinumab, and rilonacept, which target interleukin-1 to reduce its activity. Anakinra is an IL-1 receptor antagonist; canakinumab is a recombinant antihuman IL-1β monoclonal antibody that prevents human IL-1β from binding to its receptor; rilonacept is a recombinant cytokine trap that binds both IL-1α and IL-1β and prevents binding to receptors. In the treatment of CAPS, both canakinumab and rilonacept are approved for treatment of FCAS and MWS; canakinumab has approval for use in children as young as 4 years, and rilonacept is approved for use in children 12 years and older. Anakinra is approved for treatment of NOMID. Each agent has additional unique indications such as anakinra's indication for treatment of rheumatoid arthritis (RA) and canakinumab for treatment of gout flares. The 2015 practice parameter from the American Academy of Allergy, Asthma, and Immunology (AAAAI) recommends any of the 3 agents for CAPS and does not specify one agent over another for use in a particular type of CAPS. An advantage of anakinra over the other agents is its availability as a prefilled syringe. Both canakinumab and rilonacept are available as single-dose vials, and rilonacept requires reconstitution, which may be a hindrance to adherence or lead to inappropriate administration. All agents require subcutaneous administration; however, canakinumab is dosed every 8 weeks which may be an advantage over the weekly frequency of rilonacept and daily administration of anakinra. Increased monitoring of anakinra adverse events is required in patients with renal impairment. Close monitoring of adverse events and drug concentration levels of agents with a narrow therapeutic window may be required when canakinumab and rilonacept are used with certain CYP450 substrates.

	Evidence directly comparing the CAPS agents is limited. Randomized, non-randomized, and observational studies of individual agents have demonstrated improvement in clinical and laboratory outcomes with all 3 agents. Continued clinical response with has been demonstrated for up to 3 years with canakinumab, for up to 1.5 years with rilonacept, and for 5 years with anakinra. Infection is a common side effect for all 3 agents. Canakinumab appears to have less frequency of injection-site reactions, and rilonacept may increase lipid levels. Canakinumab can cross the placenta; therefore, the use of live vaccines may need to be delayed in infants. Due to the differences in multiple, labeled indications, formulations, frequency of dosing, required dose adjustments based on renal impairment, and drug interactions, the choice of treatment of CAPS should be individualized. Therefore, preference of one agent over the other cannot be generalized. Given that the existing guideline does not place preference of one agent over another for use in CAPS, preferred drugs list status may remain with the most cost-effective agents.

Table 1. Cytokine and CAM Antagonists: CAPS Agents

Generic Name	Brand Name	Approved Indications	Route of Administration	Biosimilar Availability
Anakinra	Kineret®	RA, NOMID, DIRA	Subcutaneous injection	N
Canakinumab	Ilaris®	FCAS, MWS, TRAPS, HIDS/MKD, FMF, Still's disease, Gout flares	Subcutaneous injection	N
Rilonacept	Arcalyst®	FCAS, MWS, DIRA, RP	Subcutaneous injection	N

Abbreviations: DIRA, deficiency of Interleukin-1 receptor antagonist; FCAS, familial cold auto-inflammatory syndrome; FMF, familial Mediterranean fever; HIDS/MKD, hyperimmunoglobulin; MWS, Muckle-Wells Syndrome; NOMID, neonatal multisystem inflammatory disease; RA. rheumatoid arthritis; RP, recurrent pericarditis; TRAPS, TNF receptor associated periodic syndrome.

All authorizations must be prescribed in accordance with FDA approved labeling. Use of samples to initiate therapy does not meet step therapy and/or continuation of therapy prior authorization requirements. Prior therapies will be verified through pharmacy claims and/or submitted chart notes

Initial Therapy – One of the following must be met:

- Claim is for a preferred agent **OR**

Criteria for Kineret:

- Prescribed by or in consultation with a rheumatologist, hematologist or any other specialist familiar with the treated disease state **AND**
- Documented diagnosis of deficiency of Interleukin-1 receptor antagonist (DIRA) (confirmed by genetic testing biallelic pathogenic variants in IL 1 RN gene) **OR**
- Documented diagnosis of Neonatal-onset multisystem inflammatory disease **OR**
- For a documentation of rheumatoid arthritis (RA):
  - Participant is age 18 years or older **AND**
  - Patient has had an adequate trial (30 days) of DMARD therapy, including a TNF inhibitor **AND**
- Not used in combination with another targeted immunomodulator

Criteria for Arcalyst:

- Prescribed by or in consultation with a rheumatologist, hematologist or any other specialist familiar with the treated disease state **AND**
- Documented diagnosis of DIRA (confirmed by genetic testing biallelic pathogenic variants in IL 1 RN gene) **AND**
    - Patient documented weight is 10 kg or more
    - Utilization is for the maintenance of remission of DIRA following previous treatment with Kineret (documentation required of trial)

  OR
- Patient aged 12 years or older and **ONE** of the following:
    - Documented diagnosis of CAPS **OR**
    - Documented diagnosis of recurrent pericarditis (a second instance of pericarditis after having no symptoms for at least four weeks) **AND**
- Not used in combination with another targeted immunomodulator

Criteria for Ilaris:

- Prescribed by or in consultation with a rheumatologist, hematologist or any other specialist familiar with the treated disease state **AND**
- Documented diagnosis of systemic juvenile idiopathic arthritis and both of the following:
    - Patient age 2 years or older
    - Adequate trial of tocilizumab or documented adverse event/adverse reaction or contraindication to tocilizumab (30 days) **OR**
- Documented diagnosis of CAPS and patient age 4 years or older **OR**
- Documented diagnosis of period fever syndromes (e.g., FMF, TRAPS, HIDS/MKD) in patients aged 2 years and older **OR**
- Documented diagnosis of adult-onset stills disease in patients aged 18 years and older **OR**
- Documented diagnosis of gout and documented contraindication, intolerance or inadequate response to nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine or when repeated courses of corticosteroids are not appropriate

Initial PA length: 1 year

Continuation Therapy: Documented compliance on current therapy regimen **AND** Documentation of continued clinical benefit

Continuation Length: 1 year

References:

1. Drugs@FDA: FDA Approved D rug Products. Accessed June 2025. https://www.accessdata.fda.gov/scripts/cder/daf/
2. DailyMed: National Library of Medicine. Accessed June 2025. https://dailymed.nlm.nih.gov/dailymed/index.cfm
3. Kuemmerle-Deschner JB, Gautam R, George AT, Raza S, Lomax KG, Hur P. Systematic literature review of efficacy/effectiveness and safety of current therapies for the treatment of cryopyrin-associated periodic syndrome, hyperimmunoglobulin D syndrome and tumour necrosis factor receptor-associated periodic syndrome. RMD Open. 2020 Jul;6(2):e001227.
4. Arnold DD, Yalamanoglu A, Boyman O. Systematic Review of Safety and Efficacy of IL-1-Targeted Biologics in Treating Immune-Mediated Disorders. Front Immunol. 2022 Jul 6;13:888392.
5. Romano M, Arici ZS, Piskin D, Alehashemi S, Aletaha D, Barron K, Benseler S, Berard RA, Broderick
6. L, Dedeoglu F, Diebold M, Durrant K, Ferguson P, Foell D, Hausmann JS, Jones OY, Kastner D, Lachmann HJ, Laxer RM, Rivera D, Ruperto N, Simon A, Twilt M, Frenkel J, Hoffman HM, de Jesus AA, Kuemmerle-Deschner JB, Ozen S, Gattorno M, Goldbach-Mansky R, Demirkaya E. The 2021

EULAR/American College of Rheumatology Points to Consider for Diagnosis, Management and Monitoring of the Interleukin-1 Mediated Autoinflammatory Diseases: Cryopyrin-Associated Periodic Syndromes, Tumour Necrosis Factor Receptor-Associated Periodic Syndrome, Mevalonate Kinase Deficiency, and Deficiency of the Interleukin-1 Receptor Antagonist. Arthritis Rheumatol. 2022 Jul;74(7):1102-1121.
7. Bonilla FA, Khan DA, Ballas ZK, et al: Joint Task Force on Practice Parameters, representing the American Academy of Allergy, Asthma & Immunology; the American College of Allergy, Asthma & Immunology; and the Joint Council of Allergy, Asthma & Immunology. Practice parameter for the diagnosis and management of primary immunodeficiency. J Allergy Clin Immunol. 2015;136(5):1186-205.e1-78.

Revision History

Date	Version	Revisions
11/7/2025	V1	Document approved by DSS

