



Medication Policy Manual

Policy No: dru186

Topic: Ilaris[®], canakinumab

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Next Review Date: July 2012

IMPORTANT REMINDER

This Medical Policy has been developed through consideration of medical necessity, generally accepted standards of medical practice, and review of medical literature and government approval status.

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control.

The purpose of medical policy is to provide a guide to coverage. Medical Policy is not intended to dictate to providers how to practice medicine. Providers are expected to exercise their medical judgment in providing the most appropriate care.

Description

Canakinumab (Ilaris[®]) is a subcutaneously administered medication similar to anakinra (Kineret[®]) and rilonacept (Arcalyst[®]) that blocks the activity of interleukin-1 (IL-1), a protein involved in inflammation. It is used to treat cryopyrin-associated periodic syndromes (CAPS), a group of rare inflammatory diseases.

Policy/Criteria

I. Most contracts require prior authorization approval of canakinumab prior to coverage. Canakinumab may be considered medically necessary in patients with cryopyrin-associated periodic syndromes (CAPS) when criteria A, B and C below are met.

A. There is laboratory evidence of a genetic mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1 – sometimes referred to as the NLRP3).

AND

B. There is clinical documentation that the patient is experiencing the classic symptoms of CAPS, defined as meeting either criterion 1 or 2 below:

1. Familial Cold Auto-Inflammatory Syndrome (FCAS) – Recurrent intermittent episodes of fever and rash that primarily followed natural, artificial (e.g., air conditioning) or both types of generalized cold exposure.

OR

2. Muckle-Wells Syndrome (MWS) – Syndrome of chronic fever and rash that may wax and wane in intensity; sometimes exacerbated by generalized cold exposure. This syndrome may be associated with deafness or amyloidosis.

AND

C. There is clinical documentation of significant functional impairment leading to limitations in activities of daily living (ADLs).

II. Administration, Quantity Limitations, and Authorization Period

A. RegenceRx does not consider canakinumab to be a self-administered medication.

B. When prior authorization is approved, canakinumab may be authorized in quantities of 1 vial (180 mg) per every 8 weeks (i.e. 7 vials in a 12 month period).

C. Authorization shall be reviewed as follows to confirm that current medical necessity criteria are met and that the medication is effective.

1. **Initial authorization** shall be reviewed at 1 month.

2. **Continued authorization** shall be reviewed at least annually, and documentation (including chart notes) indicating that there is disease stability or improvement must be provided.

III. Canakinumab is considered investigational when used for all other conditions including, but not limited to:

- A. Diabetes Mellitus Type 1 or Type 2.
- B. Familial Mediterranean Fever (FMF).
- C. Gout.
- D. Rheumatoid Arthritis.
- E. Systemic Juvenile Idiopathic Arthritis.

Position Statement

Summary

- CAPS are a group of rare genetic diseases affecting approximately 200 to 300 people in the United States, attributed to a specific genetic mutation.^[1]
- Two types of CAPS are recognized that affect the majority of patients^[1]
 - * Familial Cold Auto-Inflammatory Syndrome (FCAS) – Recurrent intermittent episodes of fever and rash that primarily followed natural, artificial (e.g., air conditioning) or both types of generalized cold exposure.
 - * Muckle-Wells Syndrome (MWS) – Syndrome of chronic fever and rash that may wax and wane in intensity; sometimes exacerbated by generalized cold exposure. This syndrome may be associated with deafness or amyloidosis.
- Medications that affect interleukin-1 (IL-1) may be helpful in controlling the symptoms of CAPS.
 - * Medications that affect IL-1 include anakinra, rilonacept, and canakinumab.^[1-3]
 - * Rilonacept and canakinumab have FDA marketing approval for this use.^[2,3]
 - * Because the disease is so rare, it has been difficult to conduct reliable scientific studies.
- There have been no head-to-head trials comparing the efficacy of anakinra, rilonacept, or canakinumab against each other or any other medication in the management of CAPS.
- There is currently no reliable evidence that rilonacept or canakinumab are efficacious in patients who do not exhibit the NLRP3 (CIAS1) genetic mutation.

Clinical Efficacy

- One reliable clinical trial evaluated the effectiveness of canakinumab in 35 patients with CAPS. In phase 1, all patients received a single dose of canakinumab ^[2,4]. Those who remained relapse-free after 8 weeks and elected to continue (n=31) were then randomized to receive canakinumab 150 mg SC every 8 weeks (n=15) or placebo (n=16) for up to 24 weeks. Any patient who relapsed or completed 24 weeks of therapy were then enrolled in an open-label, follow-on trial for at least two doses and up to 52 weeks of therapy.
- Of the 35 patients initially enrolled, 34 remained relapse-free for 8 weeks. ^[2,4]
- During the double-blinded, randomized phase, all subjects in the canakinumab group remained relapse-free versus 29% of subjects in placebo group at 24 weeks (100% vs 29%, $p < 0.001$, NNT = 2). ^[2,4]
- Changes in laboratory markers of inflammatory disease (CRP and SAA) were supportive of clinical findings. ^[2,4]

Safety

- The most common adverse reactions reported by patients with CAPS who were treated with canakinumab are nasopharyngitis, diarrhea, influenza, headache and nausea. ^[2,4]
- Serious adverse events include an increased incidence of serious infections and vertigo. ^[2,4]

Dosing

- Canakinumab is administered every eight weeks as a single dose via subcutaneous injection. ^[2]
- The recommended dose of canakinumab is 150 mg for CAPS patients with body weight greater than 40 kg. ^[2]
- For CAPS patients with body weight between 15 kg and 40 kg, the recommended dose is 2 mg/kg. ^[2]
- For children 15 to 40 kg with an inadequate response, the dose can be increased to 3 mg/kg. ^[2]
- Healthcare providers should perform administration of canakinumab by the subcutaneous injection route. ^[2]

OTHER USES

- Canakinumab was studied in an eight week phase II, single-blind, double-dummy, dose-ranging study against triamcinolone acetate in 299 patients with acute gouty arthritis. The results suggest that canakinumab may provide rapid and sustained pain relief, and reduce the risk of recurrent flares as compared to triamcinolone. ^[5] However, better designed randomized controlled trials are needed to establish safety and efficacy.
- Canakinumab is also currently being studied in multiple conditions including diabetes mellitus, familial Mediterranean fever, gout, rheumatoid arthritis, and systemic juvenile idiopathic arthritis. Results from these studies are not yet available. ^[6]

Cross References
Arcalyst [®] , rilonacept, dru159

Codes	Number	Description
HCPCS	J0638	Injection, canakinumab, 1 mg

References

1. Nigrovic, PA. Cryopyrin-associated periodic syndromes and related disorders. In: UpToDate, Basow, DS (Ed). UpToDate, Waltham, MA, 2010.
2. Ilaris [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; June 2009.
3. Arcalyst [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; June 2010.
4. Lachmann, HJ, Kone-Paut, I, Kuemmerle-Deschner, JB, et al. Use of canakinumab in the cryopyrin-associated periodic syndrome. *N Engl J Med*. 2009 Jun 4;360(23):2416-25. PMID: 19494217
5. So A, De Meulemeester M, Pikhlak A, et. al. Canakinumab for the treatment of acute flares in difficult-to-treat gouty arthritis: results of a multicentere, phase II, dose-ranging study. *Arthritis Rheum*. 2010 Oct;62(10):3064-76.
6. National Institutes of Health, Clinicaltrials.gov. [cited May 24, 2011]; Available from: <http://www.clinicaltrials.gov>