Medication Policy Manual

**Policy No:** dru159

**Topic:** Arcalyst®, rilonacept (Arcalyst)

**Date of Origin:** July 18, 2008

**Committee Approval Date:** September 8, 2017

**Next Review Date:** September 2018

**Effective Date:** October 1, 2017

**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**

Rilonacept (Arcalyst®) is a subcutaneously administered medication similar to anakinra (Kineret®) 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 rilonacept (Arcalyst) prior to coverage. Rilonacept (Arcalyst) 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 NLRP-3).

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. OmedaRx considers rilonacept (Arcalyst) to be a self-administered medication.

B. When prior authorization is approved, rilonacept (Arcalyst) may be authorized in quantities as follows:

1. Initial Authorization – Rilonacept (Arcalyst) may be covered in quantities up to 8 vials containing 220 mg each in the first four-week period.

2. Continued Authorization – When continued authorization is approved, rilonacept (Arcalyst) may be authorized in quantities of up to 220 mg per week.

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. Rilonacept (Arcalyst) is considered investigational when used for all other conditions including, but not limited to:

A. Atherosclerotic coronary artery disease
B. Bursitis
C. Diabetes Mellitus Type 1
D. Familial Mediterranean Fever (FMF)
E. Gout
F. 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
  * 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.[1]
  * Medications that affect IL-1 include anakinra, rilonacept (Arcalyst), and canakinumab.
  * Rilonacept (Arcalyst) and canakinumab have FDA marketing approval for this use.
  * Because the disease is so rare, it has been difficult to conduct high quality scientific studies.

- There have been no head-to-head trials comparing the efficacy of anakinra (Kineret), rilonacept (Arcalyst), or canakinumab against each other or any other medication in the management of CAPS.

- There is currently no high quality evidence that rilonacept (Arcalyst) or canakinumab are efficacious in patients who do not exhibit the NLRP3 (CIAS1) genetic mutation.

- Rilonacept (Arcalyst) provides a modest improvement in the symptoms of patients with CAPS, a rare genetic disease affecting about 200 to 300 people in the United States.[1]
  * Patients treated with rilonacept (Arcalyst) experienced reduction of mean symptom score of about 2 points (on a 10 point scale) after treatment for 24 weeks.
  * Mild to moderate injection site reactions lasting approximately one day are common after an injection of rilonacept (Arcalyst).
**Clinical Efficacy**

- One randomized, controlled study compared rilonacept (Arcalyst) to placebo in 47 patients randomized to receive either rilonacept (Arcalyst) (n = 23) or placebo (n = 24) in a blinded fashion for six weeks. All patients were tested and found to be positive for the CIAS1 mutation. At the end of six weeks, patients receiving placebo received active drug, while patients randomized to rilonacept (Arcalyst) continued with treatment in a single blinded fashion. [2-4]

- At 6 weeks, the symptom scores of patients assigned to rilonacept (Arcalyst) had improved by 2.3 points (on a 10 point scale) relative to patients receiving placebo.

- This modest benefit was sustained for up to 24 weeks of treatment during the clinical trial. A similar benefit (compared to baseline) was seen when patients continued treatment through an open-label extension up to 48 weeks.

- Subjects withdrawn from rilonacept (Arcalyst) following Part A of the trial had a return of symptoms, while those continuing on rilonacept (Arcalyst) maintained their response to treatment.

- Improvement in laboratory test results for inflammatory markers of disease (serum amyloid A and C-reactive protein) were supportive of clinical improvement seen with rilonacept (Arcalyst). These inflammatory markers are not specific to CAPS (i.e., not diagnostic), but might be useful in monitoring clinical response to treatment.

**Safety**

- Mild to moderate injection site reactions lasting approximately one day are common after an injection of rilonacept (Arcalyst). [2-4]

- Rilonacept (Arcalyst) should not be used in patients with a chronic or active infection.

- Rilonacept (Arcalyst) contains a warning for serious infections were seen during the pivotal trial. However, two patients receiving rilonacept (Arcalyst) have experienced serious infection (one resulting in death), so its use is associated with increased risk of serious infection. [2-4]

**Dosing**

- **Adult patients 18 years and older:** Treatment should be initiated with a loading dose of 320 mg delivered as two 2 mL subcutaneous injections of 160 mg each given on the same day at two different sites. Dosing should be continued with a once-weekly injection of 160 mg administered as a single 2-mL subcutaneous injection. [4]

- **Pediatric patients aged 12 to 17 years:** Treatment should be initiated with a loading dose of 4.4 mg/kg, up to a maximum of 320 mg, delivered as one or two subcutaneous injections with a maximum single-injection volume of 2 mL. Dosing should be continued with a once-weekly injection of 2.2 mg/kg, up to a maximum of 160 mg, administered as a single subcutaneous injection of up to 2 mL. [4]

- Rilonacept (Arcalyst) should not be given more often than once weekly. [4]

- Maintenance doses greater than 160 mg weekly have not been clinically evaluated.
Other Uses

- A Cochrane systematic review evaluated interleukin-1 inhibitors for the treatment of acute gout and concluded that there is low-quality evidence indicated that compared with maximum doses of indomethacin (50 mg three times a day), 320 mg of rilonacept (Arcalyst) may provide less pain relief with a similar rate of adverse events. [5]

- Rilonacept (Arcalyst) was studied in a 16-week, randomized, placebo-controlled study of 241 adult patients with chronic active gouty arthritis who were initiating uric acid-lowering therapy with allopurinol. In addition to allopurinol daily, patients received 16 once-weekly injections of rilonacept (Arcalyst) (80 mg or 160 mg) or placebo. There was a reported improvement in the number of gout flares per patient through week 16 (primary endpoint) with rilonacept (Arcalyst) vs placebo (P < 0.001). [6]

- Rilonacept (Arcalyst) versus triamcinolone was studied for the treatment of subacromial bursitis in a randomized, non-inferiority, unblinded study. While both treatments improved QuickDASH score, a measure of physical function and pain, triamcinolone offered greater improvement. [7]

- Rilonacept (Arcalyst) was studied in 14 patients ages 4 years and older with familial Mediterranean fever (FMF) who had 1 or more attacks per month and were colchicine resistant or intolerant. Patients were randomized to rilonacept (Arcalyst) 2.2 mg/kg (max 160 mg) weekly or weekly placebo for two 3-month treatment courses, and then received the other intervention for two 3-month treatment courses. Reduced frequency of FMF attacks was reported when patients were on rilonacept (Arcalyst) therapy vs placebo therapy (P = 0.004). [8] Larger, well-designed trials are needed to establish the efficacy of rilonacept (Arcalyst) in FMF.

- Rilonacept (Arcalyst) was studied in 24 systemic juvenile idiopathic arthritis (SJIA) patients in a double-blind, 4-week trial followed by an open-label phase for 23 months in 23 of these patients. Patients received 2.2 mg/kg or 4.4 mg/kg of rilonacept (Arcalyst). Improvements in clinical and laboratory measures of articular and systemic manifestations of SJIA were achieved in > 50% of rilonacept (Arcalyst)-treated patients over two years. Larger, well-designed trials are needed to establish the efficacy of rilonacept (Arcalyst) in SJIA. [9]

- Rilonacept (Arcalyst) is also currently being studied in multiple other conditions including atherosclerotic coronary artery disease, and diabetes mellitus type 1. Results from these studies are not yet available.

**Cross References**

Ilaris®, canakinumab, Medication Policy Manual, dru186
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<th>Description</th>
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<td>HCPCS</td>
<td>J2793</td>
<td>Injection, rilonacept, 1 mg</td>
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References


4. Arcalyst® [prescribing information]. Tarrytown, NY: Regeneron; September 2014


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<tr>
<th>Revision Date</th>
<th>Revision Summary</th>
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<tbody>
<tr>
<td>9/8/2017</td>
<td>No criteria changes with this annual review.</td>
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<tr>
<td>10/21/2016</td>
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