

**Regence BlueCross BlueShield of Oregon • Regence BlueShield  
Regence BlueCross BlueShield of Utah • Regence BlueShield of Idaho  
Independent licensees of the Blue Cross and Blue Shield Association**

**Medication Policy Manual**

**Policy No:** dru159

**Topic:** Arcalyst<sup>®</sup>, rilonacept

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

**Revised/Effective Date:** July 17, 2009

**Next Review Date:** July 2010

**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<sup>®</sup>), is a medication similar to anakinra (Kineret<sup>®</sup>), and blocks the activity of interleukin-1 (IL-1), a protein involved in inflammation. It is given as a subcutaneous injection and is used to treat cryopyrin-associated periodic syndromes (CAPS), a rare inflammatory disease.

## Policy/Criteria

**I.** Most contracts require prior authorization approval of rilonacept prior to coverage. Rilonacept 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 in 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 of activities of daily living (ADLs).

**II.** Administration, Quantity Limitations, and Authorization Period

**A.** Regence considers rilonacept to be a self-administered medication.

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

**1. Initial Authorization** – Rilonacept 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 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.** Riloncept is considered investigational when used for all other conditions.

## **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.
- 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.
  - \* Medications that affect IL-1 include anakinra, riloncept, and canakinumab.
  - \* Riloncept and canakinumab have FDA marketing approval for this use. <sup>[1-3]</sup>
  - \* 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, riloncept, or canakinumab against 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.
- Rilonacept provides a modest improvement in the symptoms of patients with cryopyrin-associated periodic syndromes (CAPS), a rare genetic disease affecting about 200 to 300 people in the United States.
  - \* Patients treated with rilonacept 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.
- There is currently no available evidence that rilonacept is efficacious in patients who do not exhibit the CIAS1 genetic mutation.

## *Clinical Efficacy*

One randomized, controlled study compared rilonacept to placebo in 47 patients randomized to receive either rilonacept (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 continued with treatment in a single blinded fashion<sup>[1,2,6]</sup>

- While suggestive, the results presented below are uncertain due to problems with the study design, including administration of other drugs that could affect symptoms, lack of details on how the study was blinded, and some patients receiving the wrong treatment for part of the study.
- At 6 weeks, the symptom scores of patients assigned to rilonacept had improved by 2.3 points (on a 10 point scale) relative to patients receiving placebo.
- This modest benefit was sustained 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 following Part A of the trial had a return of symptoms, while those continuing on rilonacept 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. 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.
- Rilonacept should not be used in patients with a chronic or active infection.
- No serious infections were seen during the pivotal trial. However, two patients receiving rilonacept have experienced serious infection (one resulting in death), so its use is associated with increased risk of serious infection.

## *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.
- **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, up to 2 mL.
- Rilonacept should not be given more often than once weekly.
- Maintenance doses greater than 160 mg weekly have not been clinically evaluated.

## **References**

1. Drugs@FDA [page on the internet]. FDA review documents for riloncept (Arcalyst). Available at: <http://www.fda.gov/cder/foi/nda/2008/125249s000TOC.htm>. Accessed 05/15/2008.
2. Arcalyst [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; February 2008
3. Arcalyst (riloncept) injection for subcutaneous use in the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS). [CD-ROM]. Regeneron Pharmaceuticals; 2008. Reviewed May 2008.
4. Cryopyrin-Associated Periodic Syndromes (CAPS) and its impact on patients. [CD-ROM]. Regeneron Pharmaceuticals; 2008. Reviewed May 2008.
5. FDA approves new orphan drug for treatment of rare inflammatory syndromes. News Release available at <http://fda.gov/bbs/topics/NEWS/2008/NEW01801.html>. Accessed March 20, 2008.
6. 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 Aug;58(8):2443-52.

<b>Cross References</b>
Ilaris <sup>®</sup> , canakinumab druXXX

<b>Codes</b>	<b>Number</b>	<b>Description</b>
HCPCS	J3590	Unclassified biologics