



CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

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Subject Riloncept (Arcalyst™)

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Hyperlink to Related Coverage Policies

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2010 CIGNA

Coverage Policy

CIGNA covers riloncept (Arcalyst™) as medically necessary for the treatment of CAPS (Cryopyrin-Associated Periodic Syndromes) including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older.

FDA Approved Indications

Arcalyst (riloncept) is an interleukin-1 blocker indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older.

FDA Recommended Dosing

Adult patients 18 yrs and older: Initiate treatment with a loading dose of 320 mg delivered as two, 2-mL, subcutaneous injections of 160 mg on the same day at two different sites. Continue dosing with a once weekly injection of 160 mg administered as a single, 2-mL, subcutaneous injection. Do not administer Arcalyst more often than once weekly.

Pediatric patients aged 12 to 17 years: Initiate treatment 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. Continue dosing 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. If the initial dose is given as two injections, they should be given on the same day at two different sites. Do not administer Arcalyst more often than once weekly.

Drug Availability

Arcalyst is available as a sterile, single-use 20-mL, glass vial containing 220mg of riloncept as a lyophilized powder for reconstitution.

General Background

Disease Overview

Cryopyrin-Associated Periodic Syndromes are a group of rare, autosomal dominant autoinflammatory diseases. Urticarial-like rash, fever, and joint pain are common characteristics of CAPS. These disorders are associated with mutations in the NLRP-3 gene which encodes the protein cryopyrin. Cryopyrin aids in converting IL-1 beta into its active form. The gene mutation of NLRP-3 causes increased cryopyrin activity. This causes overproduction of activated IL-1 beta, which leads to inflammation. Familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome are two types of CAPS disorders.

Familial cold autoinflammatory syndrome attacks are precipitated by exposures to cold temperatures. Symptoms of FCAS, which includes urticarial-like rash, fever, conjunctivitis, and arthralgias, generally present during the first 6 months of life. Rashes typically occur 1-2 hours after exposure to cold temperatures and lasts for approximately 12 hours. These same dermatologic and systemic manifestations typically last longer (24 – 48 hours) with Muckle-Wells syndrome. Sensorineural hearing impairment, amyloidosis, and nephropathy are other distinguishing features of Muckle-Wells syndrome.

Pharmacology

FCAS and MWS are two types of CAPS disorders for which there are limited treatment options. Riloncept blocks IL-1 beta and to a lesser extent IL-1 alpha from interacting with cell surface receptors. This reduces IL-1 mediated inflammation associated with CAPS. Steady state concentrations are achieved at approximately 6 weeks. No differences in riloncept trough levels were detected between different age, weight, and sex groups. Other pharmacokinetic data are not available.

Clinical Efficacy

A two-part double-blind, placebo-controlled, randomized trial was conducted to determine the efficacy of riloncept in patients with FCAS and MWS. The main outcome measure was the change from baseline in patient-rated mean symptom scores. Symptoms assessed were joint pain, fatigue, rash, eye redness/pain, and fever or chills. The riloncept group reported a statistically greater decrease in symptom score from baseline (-2.4) compared to placebo (-0.5, $p < 0.0001$) during the first part of the trial. In the second part ($n = 45$), all patients were treated with riloncept for 9 weeks, followed by 9 more weeks of riloncept or withdrawal with placebo. Mean symptom scores increased more in patients who were switched to placebo from riloncept (0.9) compared to those who remained on riloncept (0.1, 95% CI -1.3 to -0.4).

Adverse Reactions

Injection-site reactions were the most commonly reported adverse event. The incidence of upper respiratory tract infection was greater with riloncept compared to placebo. Most injection site-reactions were not serious, resolving within 1 to 2 days. Riloncept is also associated with increases in blood cholesterol and triglycerides. Concomitant administration of riloncept with tumor necrosis factor blockers or other IL-1 blocking agents is not recommended due to an increased risk for serious infections or neutropenia. Administer all necessary vaccines prior to beginning treatment with riloncept.

Ongoing Studies / Off-Label Uses

Recent studies suggest that blockade of the NLRP3 (cryopyrin) inflammasome interleukin 1beta (IL1beta) pathway may offer a new treatment strategy for gout. This 14-week, multicentre, non-randomised, single-blind, monosequence crossover study of 10 patients with chronic active gouty arthritis included a placebo run-in (2 weeks), active riloncept treatment (6 weeks) and a 6-week post-treatment follow-up. Riloncept was generally well tolerated. No deaths and no serious adverse events occurred during the study. One patient withdrew owing to an injection-site reaction. Patients' self-reported median pain visual analogue scale scores significantly decreased from week 2 (after the placebo run-in) to week 4 (2 weeks of riloncept) (5.0 to 2.8; $p < 0.049$), with sustained improvement at week 8 (1.3; $p < 0.049$); 5 of 10 patients reported at least a 75% improvement. Median symptom-adjusted and severity-adjusted joint scores were significantly decreased. High-sensitivity C-reactive protein levels fell significantly. This proof-of-concept study demonstrated that riloncept is generally well

tolerated and may offer therapeutic benefit in reducing pain in patients with chronic refractory gouty arthritis, supporting the need for larger, randomised, controlled studies of IL1 antagonism such as with rilonacept for this clinical indication.

Coding/Billing Information

Note: This section is not in use.

References

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