

## New Drug Bulletin:

### Rilonacept (Arcalyst™ - Regeneron Pharmaceuticals)

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Rilonacept (Arcalyst™) is a new biological product which blocks interleukin-1 (IL-1) beta from binding to cell surface receptors. Rilonacept was FDA approved in February 2008 for treating rare cryopyrin-associated periodic syndromes (CAPS) such as familial cold auto-inflammatory syndrome and Muckle-Wells syndrome. Cryopyrin-associated periodic syndromes are associated with an increase in IL-1 beta levels which result in inflammation. Rilonacept is a fusion protein product that mimics the IL-1 receptor and binds excessive IL-1 beta before it can interact with its cell surface receptor.

Rilonacept is administered as a subcutaneous injection. Average steady state trough levels of approximately 24 mcg/mL were achieved with weekly subcutaneous injections of 160 mg. Data are not available for patients with hepatic or renal dysfunction. No differences in trough concentrations were apparent with regard to differences in weight, age, or sex.

A two-part, randomized, controlled trial was conducted to determine the safety and efficacy of rilonacept. The main outcome measure was a change from baseline in patient-rated mean symptom scores (0 to 10 scale, with 0 indicating no severity and 10 indicating very severe symptoms). The symptoms rated by patients included joint pain, fatigue, rash, eye redness/pain, and fever or chills. The first part of the trial (n = 47) compared rilonacept to placebo for 6 weeks. The rilonacept group reported a statistically greater decrease in symptom score from baseline (-2.4) compared to placebo (-0.5, 95% CI -2.4 to -1.3). In the second part of the trial (n = 45), all patients were treated with rilonacept for 9 weeks, at which point patients either continued on rilonacept or were switched to placebo. Mean symptom scores increased more in patients switched to placebo from rilonacept (0.9) compared to those who remained on rilonacept (0.1, 95% CI -1.3 to -0.4).

The most common adverse reactions were injection-site reactions such as swelling, pain, redness, and itching. Injection-site reactions were greater in the rilonacept group (48%) compared to the placebo group (13%) during the first part of the two-part clinical trial. These reactions were not severe enough to cause patient discontinuation as most reactions resolved within 1 or 2 days. The second most common adverse drug reactions were infections. The overall incidence of infection among all rilonacept studies was greater in the rilonacept group (34%) than the placebo group (27%). The incidence of upper respiratory tract infection was also greater with rilonacept (48%) compared to placebo (13%). Rilonacept was also associated with increases in total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides. Monitor lipid profiles periodically in patients receiving rilonacept.

Drug interactions with rilonacept have not been studied, however concomitant administration of rilonacept with another IL-1 antagonist or a tumor necrosis factor (TNF) antagonist is not recommended due to an increased risk of serious infections and neutropenia.

No data regarding safety and efficacy of vaccines given with rilonacept are available. Give any required vaccines prior to beginning treatment with rilonacept. Rilonacept may normalize levels of cytochrome P-450 enzymes that are reduced during chronic excess IL-1 activity.

Monitor cytochrome P-450 substrates with a narrow therapeutic index in patients receiving riloncept.

The recommended dose of riloncept for adults is a subcutaneous injection of 320 mg, followed one week later by a maintenance dose of 160 mg weekly. The recommended dose for patients 12-17 years old begins with a load of 4.4 mg/kg (maximum 320 mg), followed one week later by a weekly maintenance dose of 2.2 mg/kg (maximum 160 mg). Loading doses greater than 160 mg are given as two separate subcutaneous injections administered at two different sites. No dosing recommendations are available for patients under 12 years of age.

Riloncept is available in single-use glass vials containing riloncept 220 mg. Vials must be reconstituted with 2.3 mL of sterile water for injection, yielding a riloncept concentration of 80 mg/mL. Store unreconstituted vials in the refrigerator. Reconstituted solutions are stable for 3 hours. Riloncept is currently available through two specialty pharmacies, Caremark and Accredo. No average wholesale price is available for this agent.

In summary, riloncept is an interleukin-1 (IL-1) inhibitor labeled for the treatment of CAPS in adults and children greater than 12 years of age. It is the first agent FDA-approved to treat these disorders, which include familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome.

**References:**

1. Arcalyst™ (Riloncept) package insert. Tarrytown, NY. Regeneron Pharmaceuticals, Inc.; 2008.

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