



BlueCross BlueShield
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Arcalyst (rilonacept)

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Next Review: 04/2015

Policy

BCBSKC will provide coverage for Arcalyst when it is determined to be medically necessary because the following criteria are met.

When Policy Topic is covered:

Arcalyst may be considered **medically necessary** for the treatment of the following condition:

Cryopyrin-Associated Periodic Syndromes (CAPS) (including Familial Cold Autoinflammatory Syndrome [FCAS], Muckle-Wells Syndrome [MWS], and Neonatal Onset Multisystem Inflammatory Disease [NOMID] or chronic infantile neurological cutaneous and articular [CINCA] syndrome). Approve if the patient meets the following criteria (a or b):

- a) Approve for 2 months if the patient is ≥ 12 years of age
- b) Approve for 1 year if the patient has already been started on Arcalyst; patient has had a response, as determined by the prescribing physician; and patient is continuing therapy to maintain response/remission.

Arcalyst is indicated for the treatment of MWS or FCAS in adults and adolescents ≥ 12 years of age.¹ The usual dose is a loading dose of 320 mg in adults or a weight-based dose of 4.4 mg/kg in adolescents aged 12 to 17 years followed by a weekly dose of 160 mg for adults or a weight-based dose of 2.2 mg/kg in adolescents. In the pivotal trial, patients with CAPS who were treated with Arcalyst had statistically significant reductions in key symptom score by Week 6 compared to patients taking placebo.¹⁷ NOMID is the most severe form of CAPS. Arcalyst has not been studied specifically in NOMID; however, in clinical practice IL-1 blockade with agents such as Arcalyst, Ilaris, and Kineret have been used to treat patients with NOMID.⁵⁻⁷

When Policy Topic is not covered:

Arcalyst is considered **investigational** for the treatment of all other conditions including but not limited to:

1. **Systemic Juvenile Idiopathic Arthritis (SJIA).**⁸⁻⁹ In one study, 21 children aged 5 to 20 years with systemic JIA received either 2.2 or 4.4 mg/kg of Arcalyst or placebo for 4 weeks in the double-blind phase (still blinded).⁸ After 4 weeks of double-blind therapy or a minimum of 2 weeks if rescue in the double-blind phase was warranted, patients continued on open-label therapy with their allotted dose. At 4 weeks during the open-label phase, all 6 of the American College of Rheumatology Pediatric (ACR Ped) core variables improved – ACR Ped 30, 50, and 70 responses were 76%, 62%, and 33%, respectively. Twelve patients with a median of 42 weeks of open-label therapy had both ACR Ped 50 and 70 increased to 83%. Further studies are needed.
2. **Gout.** In a short-term, pilot study (n = 10), Arcalyst was effective in decreasing pain in patients with chronic refractory gouty arthritis.¹⁰ A double-blind, placebo-controlled, Phase III study evaluated Arcalyst for gout flare prevention during initiation of allopurinol.¹¹ Patients with chronic active gouty arthritis were excluded from the study. Patients (n = 241) were randomized in a 1:1:1 ratio to

treatment with Arcalyst 80 mg (with a loading dose of 160 mg), Arcalyst 160 mg (with a loading dose of 320 mg), or placebo dosed weekly for 16 weeks. The total number of gout flares was 23 flares in the Arcalyst 80 mg treatment group, 17 flares in the Arcalyst 160 mg treatment group, and 84 flares in the placebo group. The mean number of gout flares per patient with Arcalyst 160 mg was 0.21 (95% confidence interval [CI]: 0.09, 0.33), and Arcalyst 80 mg showed the mean number of gout flares per patient was 0.29 (95% CI: 0.12, 0.46). For both Arcalyst treatment groups, there was a statistically significant reduction compared to placebo (80% [95% CI: 57.1, 83.0] and 73% [95% CI: 66.3, 88.1] for the 160 mg and 80 mg treatment groups, respectively, compared with placebo [1.06; 95% CI: 0.71, 1.42]). A Phase II, double-blind, placebo-controlled study in patients with gout who were initiating allopurinol (n = 83) found that the mean number of gout flares was statistically significantly decreased at Week 16 in patients treated with a 320 mg loading dose of Arcalyst followed by 160 mg weekly compared to patients treated with placebo (6 total flares vs. 33 total flares; P = 0.0011).¹² Preliminary results from another Phase III study reported that Arcalyst, when used for the prevention of gout flares during initiation of allopurinol, resulted in statistically significant reductions in gout flares in patients taking Arcalyst 80 mg or Arcalyst 160 mg SC weekly compared to placebo.¹³ When reviewed by the Arthritis Advisory Committee at the FDA, an unknown benefit-risk profile, including risks of malignancy and long-term safety, were cited as concerns in the gout population.¹⁴

- 3. Familial Mediterranean Fever (FMF).** Colchicine is the standard therapy for prophylaxis of attacks and amyloid deposition in this condition and has been the most studied therapy.¹⁵ In an international patient registry (Eurofever initiative), all patients with FMF (n = 121) received colchicine with 62% and 36% achieving a complete and partial response, respectively. All patients continued on colchicine with 42 patients also being treated with NSAIDs and/or steroids with a variable response. In this patient registry, no patient was treated with Arcalyst. Arcalyst is being evaluated for the treatment of FMF.¹⁶
- 4. Concurrent biologic therapy.** Arcalyst should not be administered in combination with another biologic agent for an inflammatory condition (e.g., tumor necrosis factor [TNF] blocking agents [e.g., Cimzia® {certolizumab pegol}, Enbrel® {etanercept}, Humira® {adalimumab}, Remicade® {infliximab}, Simponi™ {golimumab}], Kineret® [anakinra], or Ilaris).¹ Arcalyst has not been used in combination with TNF blocking agents. An increased incidence of serious infections has been associated with another IL-1 blocker (anakinra) when given in combination with TNF antagonists.

Considerations

Arcalyst requires prior authorization through the pharmacy services department.

This Blue Cross and Blue Shield of Kansas City policy Statement was developed using available resources such as, but not limited to: Hayes Medical Technology Directory, Food and Drug Administration (FDA) approvals, Facts and Comparisons, National specialty guidelines, Local medical policies of other health plans, Medicare (CMS), Local providers.

Description of Procedure or Service

Arcalyst is an interleukin-1 (IL-1) blocker indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children aged 12 years and older.¹ Arcalyst, also known as IL-1 TRAP, is a recombinant dimeric fusion protein that blocks IL-1 β signaling and to a lesser extent also binds IL-1 α and IL-1 receptor antagonist (IL-1ra). IL-1 cytokine signaling is important in the pathogenesis of CAPS. *Dosage:* In adults \geq 18 years of age, therapy with Arcalyst is initiated with a loading dose of 320 mg delivered as two subcutaneous (SC) injections of 160 mg on the same day at two separate sites. Dosing is continued with 160 mg once weekly as a single injection. In adolescents aged 12 to 17 years, therapy is initiated with a loading dose of 4.4 mg/kg, up to a maximum of 320 mg, delivered as one or two SC injections with a maximum single-injection volume of 2 mL. If the initial dose is two injections, then they should be given on the same day at two separate sites. In adolescents, dosing is continued with 2.2 mg/kg, up to a maximum of 160 mg once weekly as a single injection.

Rationale

CAPS is a rare inherited inflammatory disease associated with overproduction of IL-1. CAPS encompasses three rare genetic syndromes. FCAS, MWS, and neonatal onset multisystem inflammatory disorder (NOMID) or chronic infantile neurological cutaneous and articular syndrome (CINCA) are thought to be one condition along a spectrum of disease severity.²⁻³ FCAS is the mildest phenotype and NOMID is the most severe. There are no reliable prevalence statistics for CAPS, but the estimated number of persons with CAPS in the U.S. is 200 to 500. These three disorders may be associated with mutations in the *CIAS-1* gene and have autosomal dominant inheritance. Mutations in the *CIAS-1* gene, which encodes a protein (cryopyrin), cause excess release of IL-1 β and an inflammatory response. These autoinflammatory syndromes are caused by episodes of inflammation and are distinct from autoimmune disorders. The inflammatory symptoms in these patients include atypical urticaria, rash that is worse in the evening, fever, chills, fatigue, arthralgia, and conjunctival erythema. Exacerbations or flares can be triggered by exposure to cold, stress, exercise, or other stimuli. Patients with NOMID may have sensorineural hearing impairment, increased intracranial pressure, and joint abnormalities. One fourth of patients with MWS may develop systemic AA amyloidosis which usually presents with renal impairment and nephrotic syndrome; amyloidosis is less common in the other forms of CAPS.

Ilaris[®] (canakinumab) is the only other drug besides Arcalyst that is indicated for the treatment of CAPS.⁴ Ilaris is approved in adults and children aged 4 years and older and is given every 8 weeks by SC injection. Ilaris was effective in the treatment of CAPS in patients with MWS in a double-blind, placebo-controlled trial and in patients with MWS or FCAS in an open-label trial. Like Arcalyst, Ilaris is not indicated in patients with NOMID. Kineret[®] (anakinra), a recombinant nonglycosylated form of the naturally occurring IL-1Ra, is an IL-1 antagonist that is indicated for the treatment of rheumatoid arthritis and has been used to treat various forms of CAPS.² Kineret is given by SC injection once daily. Treatment of CAPS with antihistamines, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and immunosuppressants (e.g., azathioprine, cyclosporine, mycophenolate mofetil) is usually not effective.

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Billing Coding/Physician Documentation Information

J2793 Injection, riloncept, 1 mg

Additional Policy Key Words

Policy Number: 5.02.510

Related Topics

N/A

Policy Implementation/Update Information

07/2013 New Policy titled Arcalyst (riloncept)

04/2014 Reviewed – no changes made

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