ArcaIyst® Prior Authorization Criteria

<table>
<thead>
<tr>
<th>Brand</th>
<th>Generic</th>
<th>Dosage Form</th>
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<tbody>
<tr>
<td>ArcaIyst®</td>
<td>rilonacept</td>
<td>subcutaneous injection</td>
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PROGRAM OBJECTIVES
The intent of the prior authorization (PA) criteria for ArcaIyst is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines. The PA defines appropriate use as treatment for a diagnosis included in the Food and Drug Administration (FDA) approved product labeling. The PA process discourages use of this agent as a substitute for anakinra in the treatment of rheumatoid arthritis or for off-label uses and also assures the patient is not being treated concurrently with anakinra or a tumor necrosis factor (TNF-α) antagonist.

PROGRAM FUNCTIONALITY
Electronic Edits
The overall process for a prior authorization will not allow the targeted drug to adjudicate through the claims system. When a patient requests a targeted drug listed in Table 1 below, the system will reject the claim with the message indicating that prior authorization is necessary. The Prior Authorization (PA) Criteria for Approval would then be applied to requests submitted by the patient’s practitioner for evaluation.

Table 1: Targeted Agent(s) for ArcaIyst Prior Authorization

<table>
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<tr>
<th>Agent</th>
<th>GPI (multisource code)</th>
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<tr>
<td>ArcaIyst (rilonacept 220 mg injection)</td>
<td>66450060002120 (M, N, O, or Y)</td>
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Prior Authorization (PA) Criteria for Approval
No claims for ArcaIyst will be automatically paid at the point of sale. The Prior Authorization (PA) Criteria for Approval provide the manual review process for all claims for targeted agents in this PA program.

ArcaIyst (rilonacept)
Initial and Renewal Evaluation
1. Has the patient been diagnosed with Cryopyrin-Associated Periodic Syndromes (CAPS) including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS):
   If yes, continue to 2. If no, deny.

2. Has the patient been previously treated with another IL-1 inhibitor (Kineret) or a TNF-α blocking agent (Enbrel, Remicade, Humira, Cimzia)?
   If yes, continue to 3. If no, approve for 12 months.

3. Will the previous agent be discontinued before initiating therapy with ArcaIyst?
   If yes, approve for 12 months. If no, deny.
Rilonacept is an interleukin-1 (IL-1) inhibitor indicated for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), a spectrum of hereditary periodic fever disorders associated with mutations in the cold-induced autoinflammatory syndrome 1 (CIAS-1) gene and cyropyrin, the protein which it encodes. Cryopyrin, active in circulating, infection-fighting, white blood cells, controls the production of the protein IL-1. As part of the body's infection-fighting defense system, IL-1 circulates throughout the body and can trigger inflammatory reactions when it binds to inflammatory cells. Alterations in the cyropyrin protein lead to over-production of IL-1, resulting in an inflammatory response and the symptoms of CAPS. Most, but not all, patients with CAPS have the gene mutation for altered cyropyrin, CIAS-1. In one study, 27% of patients diagnosed with CAPS tested negative for CIAS-1 mutations associated with the syndrome. Diagnosis of CAPS may be made initially based on symptoms (recurrent rash, fever/chills, joint pain, eye redness/pain, fatigue) and lab findings (elevated c-reactive protein and serum amyloid A). The PA process for rilonacept will not require genetic confirmation of disease.

Cryopyrin-Associated Periodic Syndromes consists of three phenotypically related disorders all associated with mutations in the CIAS-1 gene. The mildest form, familial cold autoinflammatory syndrome (FCAS) is characterized by intermittent cold-induced rash, with fever and arthralgia. Muckle-Wells syndrome (MWS) is characterized by urticaria, deafness, and reactive amyloid A amyloidosis. The most severe form is neonatal onset multisystem inflammatory disorder (NOMID), previously known as chronic infantile neurological cutaneous and articular syndrome (CINCA). This form presents in newborns with inflammation affecting many organ systems including the skin, joints, and central nervous system. In patients with CAPS, pruritis is usually absent or minimal. Flu-like symptoms including arthralgia, myalgia, malaise, fever and conjunctival infection are common. Patients with the more severe phenotype (NOMID) may have sensorineural hearing impairment, raised intracranial pressure and joint abnormalities. Symptoms in patients with FCAS and MWS are typically periodic whereas symptoms in patients with NOMID are continuous. Intermittent, disruptive exacerbations or flares can be triggered at any time by exposure to cooling temperatures, stress, exercise, or other unknown stimuli.

Prior to the development of rilonacept CAPS has been treated with antihistamines, nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and immunosuppressants such as azathioprine, cyclosporine, and mycophenolate mofetil. In a case study of two patients, anakinra (Kineret), a recombinant IL-1 receptor antagonist, was reported to be effective in abolishing symptoms. A follow-up study treated 15 patients with anakinra for up to 3 years. All treated patients responded with complete resolution of their symptoms. Three patients diagnosed with nephrotic syndrome achieved remission on anakinra therapy.

Rilonacept, like anakinra, is a targeted inhibitor of IL-1, the key driver of inflammation in CAPS. In the six week, double blind, placebo controlled pivotal study (N=47) submitted to the Food and Drug Administration (FDA) for product approval, change in disease activity was measured using a composite symptom score (Key Symptom Score [KSS]) composed of a daily evaluation of rash, feelings of fever/chills, joint pain, eye redness/pain, and fatigue. The primary endpoint of the study was change from baseline in the mean KSS over a 21-day period between weeks four and six. Patients treated with rilonacept experienced an improvement in overall symptom scores as compared to patients treated with placebo. (mean change from baseline to endpoint of -2.6 and -0.3 points in rilonacept compared to placebo, [95% CI; -2.4, -1.3; (p<0.0001)]. These improvements were sustained over time with continued treatment. The most common adverse reactions reported with rilonacept were injection-site reaction and upper respiratory tract infection. Interleukin-1 blockade may interfere with immune response to infections and serious, life-threatening infections have been reported in patients taking Arcalyst. Taking rilonacept with tumor necrosis factor alpha (TNF-α) inhibitors is not recommended because this may increase the risk of serious infections. Treatment with rilonacept should not be initiated in patients with active or chronic infections.
Further studies are being conducted evaluating the use of rilonacept for the treatment of atherosclerosis, non-dialysis dependent chronic kidney disease (CDK) patients with anemia, familial Mediterranean fever, juvenile rheumatoid arthritis, and prevention of gout flares.7

FDA APPROVED INDICATIONS1
The following information is taken from individual drug prescribing information and is provided here as background information only. Not all FDA-approved indications may be considered medically necessary. All criteria are found in the section “Prior Authorization Criteria for Approval.”

Arcalyst1
Arcalyst (rilonacept) 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 12 years of age and older.

REFERENCES