# PRIOR AUTHORIZATION POLICY

**POLICY:** Inflammatory Conditions – Arcalyst Prior Authorization Policy
- Arcalyst® (rilonacept subcutaneous injection – Regeneron)

**REVIEW DATE:** 01/25/2023

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## OVERVIEW

Arcalyst, an interleukin-1 blocker, is indicated for the following uses:[1]

- **Cryopyrin-associated periodic syndromes (CAPS)**, including familial cold autoinflammatory syndrome and Muckle-Wells syndrome, for treatment of patients ≥ 12 years of age.
- **Deficiency of interleukin-1 receptor antagonist (DIRA),** for maintenance of remission in patients weighing at least 10 kg.
- **Pericarditis**, for treatment of recurrent disease and reduction in risk of recurrence in patients ≥ 12 years of age.

In the pivotal trial for CAPS, patients had significant improvement in symptom scores with Arcalyst through Week 6 which were maintained through Week 15. The pivotal trial for DIRA enrolled patients with a loss of function *IL1RN* mutation who previously experienced a benefit with Kineret® (anakinra subcutaneous injection). All patients (n = 6) were in remission at Month 6 and sustained remission for the remainder of the 2-year study. In the pivotal trial for pericarditis, patients had a mean of 4.7 total episodes of pericarditis (standard deviation, ± 1.7 episodes), including the current episode. All patients who enrolled in the study were symptomatic despite treatment with standard treatment (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs], colchicine, and/or systemic corticosteroids). Patients who responded to Arcalyst during the initial 12 weeks of treatment, defined as C-reactive protein ≤ 0.5 mg/dL with minimal or no pain (daily rating pain score), were eligible for continuation in the randomized withdrawal period.

## Guidelines

*Pericarditis*

Guidelines for acute and chronic pericarditis are available from the American College of Cardiology (2020).[2] A symptom-free interval of 4 to 6 weeks and evidence of new pericardial inflammation are needed for a diagnosis of recurrent disease. For recurrent disease, controlled clinical trials support a remarkable reduction in recurrences with colchicine, which should be continued for at least 6 months. Additionally, low-dose corticosteroids are associated with a high treatment success rate. NSAIDs (e.g., aspirin, ibuprofen, indomethacin) are also listed as alternatives for recurrent disease. Immunosuppressive drugs, including azathioprine, methotrexate, and mycophenolate mofetil, are effective, well tolerated, and used as corticosteroid-sparing agents. There is also limited evidence suggesting efficacy of intravenous immunoglobulins. Although Arcalyst was not yet approved for recurrent pericarditis, the guidelines note that benefit was shown in a Phase II study, demonstrated by a decrease in chest pain and C-reactive protein levels.

## POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Arcalyst. All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Arcalyst as well as the monitoring required for adverse events and long-term efficacy, initial

approval requires Arcalyst to be prescribed by or in consultation with a physician who specializes in the condition being treated.

All reviews for use of Arcalyst for COVID-19 and/or cytokine release syndrome associated with COVID-19 will be forwarded to the Medical Director.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Arcalyst is recommended in those who meet one of the following criteria:

### FDA-Approved Indications

1. **Cryopyrin-Associated Periodic Syndromes.** Approve for the duration noted if the patient meets one of the following (A or B):
   Note: This includes familial cold autoinflammatory syndrome, Muckle-Wells Syndrome, and neonatal onset multisystem inflammatory disease or chronic infantile neurological cutaneous and articular syndrome.
   - **A)** Initial Therapy. Approve for 6 months if the patient meets the following conditions (i and ii):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** The medication is prescribed by or in consultation with a rheumatologist, geneticist, allergist/immunologist, or dermatologist.
   - **B)** Patient is Currently Receiving Arcalyst. Approve for 1 year if the patient meets BOTH of the following (i and ii):
     - **i.** Patient has been established on this medication for at least 6 months; AND
       Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).
     - **ii.** Patient meets at least one of the following (a or b):
       - **a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
         Note: Examples of objective measures include resolution of fever, improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, amyloid A), reduction in proteinuria, and/or stabilization of serum creatinine.
       - **b)** Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as fewer cold-induced attacks; less joint pain/tenderness, stiffness, or swelling; decreased fatigue; improved function or activities of daily living.

2. **Deficiency of Interleukin-1 Receptor Antagonist**. Approve for the duration noted if the patient meets one of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets all of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 10 kg (22 pounds); AND
     - **ii.** Genetic testing has confirmed a mutation in the *IL1RN* gene; AND
     - **iii.** According to the prescriber, patient has demonstrated a clinical benefit with Kineret (anakinra subcutaneous injection); AND
       Note: Examples of a clinical response with Kineret include normalized acute phase reactants; resolution of fever, skin rash, and bone pain; and reduced dosage of corticosteroids.

**iv.** The medication is prescribed by or in consultation with a rheumatologist, geneticist, dermatologist, or a physician specializing in the treatment of autoinflammatory disorders.

**B)** Patient is Currently Receiving Arcalyst. Approve for 1 year if the patient meets BOTH of the following (i and ii):

**i.** Patient has been established on this medication for at least 6 months; AND
Note: A patient who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

**ii.** Patient meets at least one of the following (a or b):

**a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include improvement in rash or skin manifestations, clinically significant improvement or normalization of serum markers (e.g., C-reactive protein, erythrocyte sedimentation rate), reduction in proteinuria, and/or stabilization of serum creatinine.

**b)** Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as improvement of skin or bone symptoms; less joint pain/tenderness, stiffness, or swelling.

**3. Pericarditis.** Approve for the duration noted if the patient meets one of the following (A or B):

**A)** Initial Therapy. Approve for 3 months if the patient meets all of the following (i, ii, iii, iv, and v):

**i.** Patient is ≥ 12 years of age; AND

**ii.** Patient has recurrent pericarditis; AND

**iii.** Prior to starting treatment with Arcalyst, the patient had a of at least three episodes of pericarditis; AND

**iv.** Patient meets one of the following (a or b):

**a)** For the current episode, the patient is receiving standard treatment; OR

**b)** Standard treatment is contraindicated; AND
Note: Standard treatments for pericarditis include nonsteroidal anti-inflammatory drug(s) [NSAIDs], colchicine, and/or systemic corticosteroids.

**v.** The medication is prescribed by or in consultation with a cardiologist or rheumatologist.

**B)** Patient is Currently Receiving Arcalyst. Approve for 1 year if the meets BOTH of the following (i and ii):

**i.** Patient has been established on this medication for at least 3 months; AND
Note: A patient who has received < 90 days of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).

**ii.** Patient meets at least one of the following (a or b):

**a)** When assessed by at least one objective measure, patient experienced a beneficial clinical response from baseline (prior to initiating the requested drug); OR
Note: Examples of objective measures include normalization of inflammatory biomarkers such as erythrocyte sedimentation rate and/or C-reactive protein, continued resolution of fever.

**b)** Compared with baseline (prior to initiating the requested drug), patient experienced an improvement in at least one symptom, such as resolution of chest pain or pericarditis pain.

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Arcalyst is not recommended in the following situations:

1. **Concurrent Biologic Therapy.** Arcalyst should not be administered in combination with another biologic agent for an inflammatory condition (see Appendix for examples).[1] Arcalyst has not been used in combination with tumor necrosis factor inhibitors (TNFis). An increased incidence of serious infections has been associated with another interleukin-1 blocker (Kineret® [anakinra subcutaneous injection]) when given in combination with TNFis.

2. **COVID-19 (Coronavirus Disease 2019).** Forward all requests to the Medical Director.
   Note: This includes requests for cytokine release syndrome associated with COVID-19.

3. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

## REFERENCES

1. Arcalyst® subcutaneous injection [prescribing information]. Tarrytown, NY: Regeneron; March 2021.
2. Chiabrando JG, Bonaventura A, Vecchie A, et al. Management of acute and recurrent pericarditis. *J Am Coll Cardiol*. 2020;75(1):76-92.
3. Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. *N Engl J Med*. 2021;384(1):31-41.

| Type of Revision | Summary of Changes | Review Date |
|---|---|---|
| Annual Revision | **Cryopyrin-Associated Periodic Syndromes:** Initial approval duration was changed to 6 months (previously was 3 months). For a patient currently receiving, it was clarified that this applies to a patient who is receiving for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years.<br>**Deficiency of Interleukin-1 Receptor Antagonist:** For a patient currently receiving, it was clarified that this applies to a patient who is receiving for ≥ 6 months. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. For continuation, approvals were changed to be 1 year in duration. Previously, response was more general and according to the prescriber, and approvals were for 3 years.<br>**Pericarditis:** For a patient currently receiving, it was clarified that this applies to a patient who is receiving for ≥ 90 days. A requirement was added for a patient who is currently receiving to have at least one objective or subjective response to therapy. Previously, response was more general and according to the prescriber. | 02/16/2022 |
| Annual Revision | No criteria changes. | 01/25/2023 |

## APPENDIX

* Not an all-inclusive list of indication (e.g., oncology indications and rare inflammatory conditions are not listed). Refer to the prescribing information for the respective agent for FDA-approved indications; SC – Subcutaneous; TNF – Tumor necrosis factor; AS – Ankylosing spondylitis; CD – Crohn's disease; JIA – Juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; UC – Ulcerative colitis; nr-axSpA – Non-radiographic axial spondyloarthritis; IV – Intravenous, PJIA – Polyarticular juvenile idiopathic arthritis; IL – Interleukin; SJIA – Systemic juvenile idiopathic arthritis; ^ Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis.