



## Drug Coverage Policy

Effective Date .....06/01/2025

Coverage Policy Number .....IP0437

Policy Title .....Arcalyst

## Inflammatory Conditions – Arcalyst

- Arcalyst® (rilonacept subcutaneous injection - Regeneron)

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### OVERVIEW

Arcalyst, an interleukin-1 (IL-1) blocker, is indicated for the following uses:<sup>1</sup>

- **Cryopyrin-associated periodic syndromes (CAPS)**, including familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS), for treatment of patients ≥ 12 years of age.

- **Deficiency of interleukin-1 receptor antagonist (DIRA)**, for maintenance of remission in adults and pediatric patients weighing at least 10 kg.
- **Pericarditis**, for treatment of recurrent disease and reduction in risk of recurrence in patients  $\geq 12$  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.<sup>1</sup> 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,  $\pm 1.7$  episodes), including the current episode.<sup>3</sup> 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  $\leq 0.5$  mg/dL with minimal or no pain (daily rating pain score), were eligible for continuation in the randomized withdrawal period.

## Guidelines

Arcalyst is used for treatment of a variety of periodic fever syndromes and inflammatory conditions.

### *CAPS and DIRA*

The European Alliance of Associations for Rheumatology (EULAR) and American College of Rheumatology (ACR) [2021] provide treatment guidelines for IL-1 mediated autoinflammatory diseases: cryopyrin-associated periodic syndromes, tumor necrosis factor receptor-associated periodic syndrome, mevalonate kinase deficiency, and deficiency of the IL-1 receptor antagonist.<sup>4</sup> Guidelines indicate IL-blocking therapy has become the preferred treatment and a therapeutic trial with IL-1 blocking agents may be started when strong clinical suspicion of a diagnosis of CAPS, TRAPS, MKD, or DIRA is suspected. The guidelines also provide additional diagnosis-specific treatment recommendations:

- **CAPS:** CAPS encompasses three rare genetic syndromes (familial cold autoinflammatory syndrome, Muckle-Wells syndrome, and neonatal onset multisystem inflammatory disease formerly known as chronic infantile neurological cutaneous and articular syndrome) that are thought to be one condition along a spectrum of disease severity. IL-1 blockers are recommended as standard of care across the spectrum of disease for improved symptom control and reduced systemic and tissue/organ inflammation. The dose and/or frequency of administration should be adjusted to control disease activity, normalize markers of systemic inflammation, and for appropriate weight gain and development in the growing patient.
- **DIRA:** DIRA is caused by recessive loss-of-function pathogenic variants in the *IL1RN* gene. Treatment with agents that block both IL- $\alpha$  and IL- $\beta$  is recommended and includes Arcalyst and Kineret.

### *Pericarditis*

Guidelines for acute and chronic pericarditis are available from the American College of Cardiology (2020).<sup>2</sup> 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.

## Coverage Policy

### POLICY STATEMENT

Prior Authorization is required for 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.

**Documentation:** Documentation will be required where noted in the criteria below. Documentation may include, but is not limited to, chart notes, laboratory records, and prescription claims records.

**Arcalyst is considered medically necessary when ONE of the following is met (1, 2, or 3):**

### FDA-Approved Indications

**1. Cryopyrin-Associated Periodic Syndromes (CAPS).** Approve for the duration noted if the patient meets ONE of the following (A or B):

Note: This includes familial cold autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and/or neonatal onset multisystem inflammatory disease (NOMID) formerly known as chronic infantile neurological cutaneous and articular syndrome (CINCA).

**A) Initial Therapy.** Approve for 6 months if the patient meets ALL of the following (i, ii, and iii):

- i. Patient is  $\geq 12$  years of age; AND
- ii. Documentation is provided that the patient has a confirmed diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS); AND
- iii. The medication is prescribed by or in consultation with a rheumatologist, geneticist, allergist/immunologist, or dermatologist; OR

**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: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.
- 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.

Note: Examples of improvement in symptoms include 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 (DIRA).** 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  $\geq 10$  kg (22 pounds); AND
- ii. Documentation is provided that the patient has had genetic testing that has confirmed bi-allelic pathogenic variants 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; OR

**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: For a patient who has not received 6 months of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.
- 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.  
Note: Examples of improvement of symptoms include an 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  $\geq 12$  years of age; AND
- ii. Patient has recurrent pericarditis; AND
- iii. Documentation is provided that the patient had a history of at least three episodes of pericarditis, prior to starting treatment with Arcalyst; 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; OR

**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: For a patient who has not received 90 days of therapy or who is restarting therapy with this medication, refer to Initial Therapy criteria above.
- 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.  
Note: Examples of improvement of symptoms include resolution of chest pain or pericarditis pain.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

### Conditions Not Covered

**Arcalyst for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):**

1. **Concurrent Biologic Therapy.** Arcalyst should not be administered in combination with another biologic agent for an inflammatory condition (see [Appendix](#) for examples).<sup>1</sup> 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.

## Coding Information

**Note:** 1) This list of codes may not be all-inclusive.  
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

HCPSC Codes	Description
J2793	Injection, rilonacept, 1 mg

## References

1. Arcalyst® subcutaneous injection [prescribing information]. Tarrytown, NY: Regeneron; November 2024.

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.
4. Romano M, Arici ZS, Piskin D, et al. The 2021 EULAR/American College of Rheumatology points to consider for diagnosis, management and monitoring of the interleukin-1 mediated autoinflammatory diseases: cryopyrin-associated periodic syndromes, tumour necrosis factor receptor-associated periodic syndrome, mevalonate kinase deficiency, and deficiency of the interleukin-1 receptor antagonist. *Ann Rheum Dis.* 2022;81(7):907-921.

## Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	<p>Updated title of the policy from Rilonacept to Inflammatory Conditions – Arcalyst.</p> <p><b>All Indications:</b> Criteria were updated to clarify “Initial Therapy” versus “Patient is Currently Receiving Arcalyst”.</p> <p><b>Cryopyrin-Associated Periodic Syndromes.</b> “Treatment of ONE of the following: Chronic infantile neurological cutaneous and articular (CINCA) syndrome, Familial Cold Autoinflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS), or Neonatal-Onset Multisystem Inflammatory Disease (NOMID)” was relocated to a Note with all of the conditions included as examples of CAPS. Updated the initial approval duration from 12 months to 6 months. Added “Patient is ≥ 12 years of age.”</p> <p><b>Deficiency of Interleukin-1 Receptor Antagonist.</b> Updated the initial approval duration from 12 months to 6 months. Added “According to the prescriber, patient has demonstrated a clinical benefit with Kineret (anakinra subcutaneous injection)” with examples of a clinical response included in a Note.</p> <p><b>Pericarditis.</b> Removed “Pericarditis secondary to the following etiologies has been ruled out: systemic autoimmune disease, infection (e.g. tuberculosis), myocarditis, trauma, radiation or cancer.”</p> <p><b>Conditions Not Covered.</b> Removed Adult Onset Still’s Disease, Gout, Juvenile Idiopathic Arthritis, Schnitzler Syndrome, and Type 1 or 2 Diabetes for list maintenance and simplification. This does not imply a change in coverage status, and all remain conditions not covered.</p>	9/1/2024

Selected Revision	<b>Added</b> HCPCS coding table <b>Added HCPCS:</b> J2793	9/1/2024
Annual Revision	<p><b>Cryopyrin-Associated Periodic Syndromes (CAPS).</b> For Initial Therapy, added "Documentation is provided that the patient has a confirmed diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS)".</p> <p><b>Deficiency of Interleukin-1 Receptor Antagonist:</b> Updated the statement "Genetic testing has confirmed a mutation in the <i>IL1RN</i> gene" to now read "Documentation is provided that the patient has had genetic testing that has confirmed bi-allelic pathogenic variants in the <i>IL1RN</i> gene."</p> <p><b>Pericarditis.</b> Added documentation requirements confirming a history of at least three episodes of pericarditis, prior to starting treatment with Arcalyst.</p> <p>Updated Appendix.</p>	05/01/2025
Selected Revision	<b>COVID-19 (Coronavirus Disease 2019):</b> Removed from Conditions Not Covered.	06/01/2025

The policy effective date is in force until updated or retired.

## APPENDIX

	Mechanism of Action	Examples of Indications*
<b>Biologics</b>		
<b>Adalimumab SC Products</b> (Humira®, biosimilars)	Inhibition of TNF	AS, CD, HS, JIA, PsO, PsA, RA, UC
<b>Cimzia®</b> (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, JIA, nr-axSpA, PsO, PsA, RA
<b>Etanercept SC Products</b> (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA, RA
<b>Infliximab IV Products</b> (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
<b>Zymfentra®</b> (infliximab-dyyb SC injection)	Inhibition of TNF	CD, UC
<b>Simponi®, Simponi Aria®</b> (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
<b>Tocilizumab Products</b> (Actemra® IV, biosimilar; Actemra SC, biosimilar)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
<b>Kevzara®</b> (sarilumab SC injection)	Inhibition of IL-6	RA
<b>Orencia®</b> (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PsA, RA
		IV formulation: JIA, PsA, RA

<b>Rituximab IV Products</b> (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
<b>Kineret®</b> (anakinra SC injection)	Inhibition of IL-1	JIA <sup>^</sup> , RA
<b>Omvoh®</b> (mirikizumab IV infusion, SC injection)	Inhibition of IL-23	UC
<b>Ustekinumab IV/SC Products</b> (Stelara®, biosimilars)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
<b>Siliq®</b> (brodalumab SC injection)	Inhibition of IL-17	PsO
<b>Cosentyx®</b> (secukinumab SC injection; secukinumab IV infusion)	Inhibition of IL-17A	SC formulation: AS, ERA, HS, nr-axSpA, PsO, PsA
		IV formulation: AS, nr-axSpA, PsA
<b>Taltz®</b> (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
<b>Bimzelx®</b> (bimekizumab-bkzx SC injection)	Inhibition of IL-17A/17F	AS, HS, nr-axSpA, PsO, PsA
<b>Ilumya®</b> (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
<b>Skyrizi®</b> (risankizumab-rzaa SC injection, risankizumab-rzaa IV infusion)	Inhibition of IL-23	SC formulation: CD, PSA, PsO, UC
		IV formulation: CD, UC
<b>Tremfya®</b> (guselkumab SC injection, guselkumab IV infusion)	Inhibition of IL-23	SC formulation: PsA, PsO, UC
		IV formulation: UC
<b>Entyvio®</b> (vedolizumab IV infusion, vedolizumab SC injection)	Integrin receptor antagonist	CD, UC

\* Not an all-inclusive list of indications. 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; HS – Hidradenitis suppurativa; 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; <sup>^</sup> Off-label use of Kineret in JIA supported in guidelines; ERA – Enthesitis-related arthritis; DMARD – Disease-modifying antirheumatic drug.

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