

## PHARMACY COVERAGE GUIDELINE

### ARCALYST® (riloncept) Generic Equivalent (if available)

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#### **This Pharmacy Coverage Guideline (PCG):**

- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively “Service”) is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider’s judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member’s benefit plan; and
- Is subject to change as new information becomes available.

#### **Scope**

- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

#### **Instructions & Guidance**

- To determine whether a member is eligible for the Service, read the entire PCG.
  - This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
  - Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
  - The “Criteria” section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member’s benefit plan.
  - The “Description” section describes the Service.
  - The “Definition” section defines certain words, terms or items within the policy and may include tables and charts.
  - The “Resources” section lists the information and materials we considered in developing this PCG
  - **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
  - Information about medications that require prior authorization is available at [www.azblue.com/pharmacy](http://www.azblue.com/pharmacy). You must fully complete the [request form](#) and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to [Pharmacyprecert@azblue.com](mailto:Pharmacyprecert@azblue.com).
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## Medical Necessity Requirements for **ARCALYST** (riloncept)

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### Criteria for Initial Therapy:

#### Prescriber Qualifications

- Prescribed by a physician specializing in the diagnosis or in consultation with a rheumatologist, geneticist, allergist, immunologist, or dermatologist (depending on the indication)

#### Indication

- Cryopyrin-Associated Periodic Syndromes (CAPS), (including Familial Cold Autoinflammatory Syndrome and Muckle-Wells Syndrome)
- Maintenance of remission of Deficiency of Interleukin-1 Receptor Antagonist

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- Recurrent pericarditis

#### Age Requirement

- 12 years or older
- **For Deficiency of Interleukin-1 Receptor Antagonist indication only:** any age and weighs at least 10 kilograms

#### Baseline Clinical Evaluation

- **For Deficiency of Interleukin-1 Receptor Antagonist, ALL** the following:
  - History of clinical features (e.g., neonatal onset of sterile multifocal osteomyelitis, periostitis, cutaneous pustulosis, nail changes, absence of infection, high-titer autoantibodies, autoreactive T cells, etc)
  - Genetic testing confirms mutation in IL1RN gene
  - Disease is in remission from previous Kineret (anakinra) treatment
- **For Recurrent Pericarditis, THREE** or more episodes of pericarditis

#### Alternative Therapies

- **For Recurrent Pericarditis:**
  - Recurrent pericarditis occurred despite failure, contraindication, intolerance to colchicine in combination with a nonsteroidal anti-inflammatory drug or corticosteroid

#### Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

#### Safety

- No evidence of active serious infections (including opportunistic infections, fungal infections, tuberculosis, localized infections, sepsis, Hepatitis B, Hepatitis C)
- No concomitant use of live vaccines
- No concomitant use with biologic immunomodulators or other potent immunosuppressants (e.g., Kineret, Ilaris, Adbry, cyclosporine, Dupixent, rituximab, infliximab, Enbrel, Otezla, Vtama, Xolair, or Janus kinase inhibitors such as Cibinqo, Olumiant, Opzelura, Rinvoq, Xeljanz, etc.)

#### Documentation Requirements

- A completed request form must be submitted, including:
  - Chart notes
  - Lab results
  - Supporting clinical documentation

#### Initial Therapy Criteria Approval Duration

- 6 months OR end of plan year

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#### Criteria for Continuation of Therapy (renewal therapy)

Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy

#### Prescriber Qualification

- Continues to be seen by a physician specializing in or is in consultation with a rheumatologist, geneticist, allergist, immunologist, or dermatologist (depending on the indication)

#### Clinical Response

- Cryopyrin-Associated Periodic Syndromes
  - Improvement in at least **TWO** signs and symptoms compared to baseline (e.g., decrease in proteinuria, serum creatinine, C-reactive protein, joint pain, fatigue, resolution of fever and rash, improvement in daily function)
- Deficiency of Interleukin-1 Receptor Antagonist
  - Maintains remission or significant improvement from baseline in at least **TWO** signs and symptoms (e.g., no rash, normalization of C-reactive protein and erythrocyte sedimentation rate, decrease in serum creatinine or proteinuria, joint pain, stiffness, swelling, improvement in skin or bone symptoms, etc.)
- Recurrent Pericarditis
  - Improvement in at least **TWO** signs and symptoms compared to baseline (e.g., C-reactive protein, erythrocyte sedimentation rate, resolution of chest pain, etc.)

#### Adherence

- Adherence to the prescribed therapy regimen has been documented

#### Brand Specific Criteria

- Have failure, contraindication or intolerance with **THREE** generic equivalents (when available) for at least three months each. **Note:** Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

#### Safety

- No evidence of active serious infections (including opportunistic infections, fungal infections, tuberculosis, localized infections, sepsis, Hepatitis B, Hepatitis C)
- No concomitant use of live vaccines
- No concomitant use with biologic immunomodulators or other potent immunosuppressants (e.g., Kineret, Ilaris, Adbry, cyclosporine, Dupixent, rituximab, infliximab, Enbrel, Otezla, Vtama, Xolair, or Janus kinase inhibitors such as Cibinqo, Olumiant, Opzelura, Rinvoq, Xeljanz, etc.)

#### Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use

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#### Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

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#### Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications
2. Off-Label Use of Cancer Medications

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#### Description:

Arcalyst (riloncept) is an interleukin-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 and older; maintenance of remission of Deficiency of Interleukin-1 Receptor Antagonist (DIRA) in adults and pediatric patients weighing 10 kg or more; and treatment of recurrent pericarditis (RP) and reduction in risk of recurrence in adults and children 12 years and older.

Cryopyrin-Associated Periodic Syndromes (CAPS) is a spectrum of three phenotypically related autoinflammatory syndromes. CAPS consists of a group of rare, autosomal dominantly inherited conditions consisting of Familial Cold Autoinflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS), Neonatal-Onset Multisystem Inflammatory Disease (NOMID, it is also known as Chronic Infantile Neurologic Cutaneous Articular (CINCA) Syndrome). CAPS is caused by Cold-Induced Auto-inflammatory Syndrome-1 (*CIAS1*) gene mutation and is characterized by recurrent symptoms (urticaria-like skin lesions, fever chills, arthralgia, profuse sweating, sensorineural hearing/vision loss, and increased inflammation markers the blood). The three conditions share many clinical features. Features common to all disorders include fever, urticaria-like rash, arthralgia, myalgia, fatigue, and conjunctivitis. NOMID is the most severe form of the three syndromes; FCAS is the mildest and most common. The boundaries among these three syndromes are not sharp, and individuals may have features of more than one disorder or may not be classic for any of them.

CAPS results from a mutation of the nucleotide-binding domain, leucine rich family, pyrin domain containing 3 (*NLRP3*) gene (it is also known as Cold-Induced Auto-inflammatory Syndrome-1 [*CIAS1*]). *NLRP3* encodes for cryopyrin, which ultimately leads to overproduction of interleukin-1, resulting in inflammatory symptoms seen in CAPS. Features include cutaneous, neurological, ophthalmologic, and rheumatologic manifestations.

Clinical symptoms usually first present in early childhood and appear similar to mild-to-moderate cases of flu or allergy. FCAS is characterized by recurrent urticaria, arthralgia, and fever after general exposure to cold. In addition to the characteristics observed in FCAS, MWS is characterized by renal amyloidosis, hearing loss, and conjunctivitis. NOMID individuals present at birth with systemic inflammation, including fever and elevation of acute-phase reactants, conjunctivitis, and an urticaria-like rash. Severe organ-specific manifestations involving the eye, severe manifestations in the central nervous system (aseptic meningitis and ventriculomegaly), and damage to bone, with benign, tumor-like lesions are seen only in NOMID individuals.

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Deficiency of the interleukin (IL) 1 receptor antagonist (DIRA) is a genetic autoinflammatory syndrome characterized by the neonatal onset of sterile multifocal osteomyelitis, periostitis, and cutaneous pustulosis as well as the absence of evidence of infection, high-titer autoantibodies, and autoreactive T cells. The cutaneous eruption manifests as discrete crops of pustules, generalized pustules, or ichthyosiform lesions and may be accompanied by nail changes. Histopathologic examination of the skin lesions in affected individuals demonstrates extensive epidermal and dermal neutrophilic infiltrates. DIRA is distinct from CAPS. DIRA presents at birth or within two months postpartum. Untreated individuals die from multiorgan failure. Marked elevations of the erythrocyte sedimentation rate and serum C-reactive protein (CRP) are present, but fever is not. Deficiency of the interleukin (IL) 1-receptor antagonist (IL-1RN) is due to homozygous germline pathogenic variants in *IL1RN* gene. Heterozygous carriers are asymptomatic. The diagnosis is made by genetic testing for mutations involving *IL1RN*. Treatment with nonsteroidal anti-inflammatory drugs, disease-modifying antirheumatic drugs, and glucocorticoids are only partially effective. IL-1 inhibitors including Kineret (anakinra), a recombinant human IL-1 receptor antagonist, and Arcalyst (rilonacept), an IL-1 trap, are approved by the US Food and Drug Administration (FDA) for treatment of DIRA.

Pericarditis is inflammation of the pericardial sac. The predominant symptoms is pleuritic chest pain. Recurrent pericarditis (RP) refers to a syndrome in which symptoms of acute pericarditis recur after the initial episode and recurrence of symptoms after a symptom-free interval of at least four to six weeks. Most RP are caused by autoimmune disorder, though a minority of cases may be caused by an infection. Colchicine in combination with an NSAID or aspirin is first line. Colchicine plus glucocorticoids are second line if an NSAID is contraindicated. Recurrence may be as high as 15 to 30 percent in patients with idiopathic acute pericarditis not treated with colchicine. Interleukin-1 inhibitors including Kineret (anakinra) (off-label) and Arcalyst (rilonacept) are options for refractory disease.

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#### **Definitions:**

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting  
[MedWatch Forms for FDA Safety Reporting | FDA](#)

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#### **Resources:**

Adler A, Imazio M. Recurrent pericarditis. In: UpToDate, Gersh BJ, Oh JK, Yeon SB (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through March 2025. Topic last updated on January 11, 2024. Accessed April 11, 2025.

Arcalyst (rilonacept) product information, revised by Kiniksa Pharmaceuticals (UK), LTD. 11/2024. Available at DailyMed <http://dailymed.nlm.nih.gov>. Accessed March 6, 2025.

Nigrovic PA. Cryopyrin-associated periodic syndromes and related disorders. In: UpToDate, Orange JS, Kaplan SL, TePas E (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through March 2025. Topic last updated on February 6, 2023. Accessed April 7, 2025.

Nigrovic PA. Interleukin 1 inhibitors: Biology, principles of use, and adverse events. In: UpToDate, O'Dell JR, Case SM (Eds), UpToDate, Waltham MA.: UpToDate Inc. Available at <http://uptodate.com>. Literature current through March 2025. Topic last updated on March 11, 2025. Accessed April 7, 2025.

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