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**Effective Date: 06/08/2023**

**Arcalyst® (riloncept)**

**HCPCS: J2793**

**Policy:**

*Requests must be supported by submission of chart notes and patient specific documentation.*

- A. Coverage of the requested drug is provided when all the following are met:
  - a. FDA approved age
  - b. Diagnosis of Cryopyrin-Associated Periodic Syndromes (CAPS) with phenotypes of Familial Cold Auto-Inflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS)
    - i. Laboratory evidence of a genetic mutation (such as in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1 – also referred to as the NLRP-3)) OR
    - ii. Elevated inflammatory markers (C-reactive protein [CRP] and serum amyloid A) plus at least two of six typical CAPS manifestations:
      - 1. Urticaria-like rash
      - 2. Cold-triggered episodes
      - 3. Sensorineural hearing loss
      - 4. Musculoskeletal symptoms
      - 5. Chronic aseptic meningitis
      - 6. Skeletal abnormalities
  - c. Diagnosis of deficiency of interleukin-1 receptor antagonist (DIRA)
    - i. Laboratory evidence of homozygous genetic mutations of IL1RN
    - ii. Trial and failure, contraindication, or intolerance to Kineret
  - d. Diagnosis of recurrent pericarditis (RP)
    - i. Trial and failure, contraindication, OR intolerance to nonsteroidal anti-inflammatory drugs (NSAIDs) in combination with colchicine
    - ii. Trial and failure, contraindication, OR intolerance to Kineret
  - e. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN utilization management medical drug list.
- B. Quantity Limitations, Authorization Period and Renewal Criteria
  - a. Quantity Limits: Align with FDA recommended dosing.
  - b. Authorization Period: One year at a time
  - c. Renewal criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit.

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\*\*\*Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

## Background Information

- Arcalyst is an interleukin(IL)-1 $\beta$  blocker indicated for the treatment of
  - Adults and children 12 years of age and older with Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Autoinflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS)
  - Maintenance of remission of deficiency of interleukin-1 receptor antagonist (DIRA) in adults and pediatric patients weighing at least 10 kg
  - Treatment of recurrent pericarditis (RP) and reduction in risk of recurrence in adults and children 12 years and older
- Cryopyrin-Associated Periodic Syndromes
  - CAPS are a group of rare genetic diseases affecting approximately 200 to 300 people in the United States, attributed to a specific genetic mutation. There are two types of CAPS recognized that affect the majority of patients.
    - FCAS patients have recurrent intermittent episodes of fever and rash that primarily follow natural, artificial (e.g., air conditioning), or both types of generalized cold exposure.
    - MWS patients have chronic fever and rash that may wax and wane in intensity. Symptoms are sometimes exacerbated by generalized cold exposure. This syndrome may be associated with deafness or amyloidosis.
  - The diagnosis of CAPS is confirmed by genetic testing for NALP3 mutations, however, in some patients, the mutation is not detectable for various reasons. In patients with no detectable NALP3 mutations, diagnostic criteria include raised inflammatory markers (C-reactive protein [CRP] and serum amyloid A) plus at least two of six typical CAPS manifestations which include urticaria-like rash, cold-triggered episodes, sensorineural hearing loss, musculoskeletal symptoms, chronic aseptic meningitis, and skeletal abnormalities.
  - Ilaris<sup>®</sup> (canakinumab) is another IL-1 $\beta$  blocker indicated for the treatment of CAPS. Both products appear to have similar efficacy. Ilaris has a more convenient dosing regimen and is indicated for a younger age population (4 years old).
- Deficiency of interleukin-1 receptor antagonist
  - DIRA is a very rare genetic autoinflammatory syndrome that presents in the first days of life. The distinctive features are inflammatory changes in the skin and bone in the absence of fever. All affected children develop a pustular rash in which there may be discrete crops of pustules or a severe generalized pustular eruption that may resemble generalized pustular psoriasis. All patients will also develop inflammation in the bones, which causes painful movement, joint swelling, and characteristic changes on x-ray. Patients may also present with fetal distress, mouth lesions, hepatosplenomegaly, generalized ichthyosis-like changes,

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pitting and separation of the nail from the nail bed, stomatitis, and conjunctivitis. If left untreated, patients may die of multisystem organ failure.

- Diagnosis of DIRA is confirmed through genetic testing for IL1RN mutations. DIRA is an autosomal recessive anti-inflammatory disease and therefore, patients should have two mutations of the IL1RM gene to exhibit symptoms. The double mutation causes an absence of interleukin-1–receptor antagonist allowing unopposed action of interleukin-1 resulting in systemic inflammation with skin and bone involvement.
- Kineret has been used as a first-line agent for the treatment of DIRA since the disease’s discovery and can be used for induction and maintenance of remission. Arcalyst has only been studied to maintain remission following induction with Kineret. There are no head to head trials to show Arcalyst is superior to Kineret once remission is reached, as such, since patients must start therapy with Kineret, it is reasonable to continue therapy with it unless an adverse reaction or contraindication is experienced.

#### - Recurrent Pericarditis

- Recurrent pericarditis refers to a syndrome in which acute pericarditis recurs after the agent inciting the original acute attack has disappeared or has ceased to be active. It is diagnosed with a documented first episode of acute pericarditis, a symptom-free interval of 4 – 6 weeks or longer, and evidence of subsequent recurrence of pericarditis, such as: chest pain, pericardial rub, fever, electrocardiogram changes, new or worsening pericardial effusion, and/or elevated markers of inflammation. The recurrence rate after an initial episode of pericarditis ranges from 15% to 30%.
- The 2015 European Society of Cardiology Guidelines for the Diagnosis and Management of Pericardial Diseases recommend therapy be targeted at the underlying etiology in patients with an identified cause with aspirin or NSAIDs remaining the mainstay of therapy. Colchicine is recommended on top of standard anti-inflammatory therapy to improve the therapeutic response, improve remission rates, and prevent recurrences.
- In cases of incomplete response to aspirin/NSAIDs and colchicine, treatment guidelines state corticosteroids may be used, but they should be added at low to moderate doses to aspirin/NSAIDs and colchicine as triple therapy. Corticosteroids should not replace these other therapies and should be used to achieve better control of symptoms. Corticosteroids at low to moderate doses should be avoided if infections cannot be excluded and should be restricted to patients with specific indications, such as, systemic inflammatory diseases, post-pericardiotomy syndromes, or pregnancy, or those with NSAID contraindications. Although corticosteroids provide rapid control of symptoms, they favor chronicity, more recurrences, and side effects. If corticosteroids are used, they should be tapered slowly. A critical threshold for recurrences is a 10 – 15 mg/day dose of prednisone or equivalent. In cases of recurrence, every effort should be made not to increase the dose or to reinstate corticosteroids.
- After obtaining a complete response, tapering should be done with a single class of drug at a time before colchicine is gradually discontinued. Recurrences are possible after discontinuation of each drug. Each tapering should be attempted only if symptoms are absent and C-reactive protein (CRP) is normal.
- Kineret has been shown to reduce the risk of further recurrences in patients with recurrent pericarditis. In the AIRTRIP trial, 21 patients with at least three episodes of recurrent pericarditis were treated with Kineret for two months. After two months, and following resolution of pericarditis symptoms, patients were randomized in a double-blind fashion to continue Kineret or switch to placebo for six months or until symptoms recurred. After a median follow-up of 14 months, patients in the Kineret group had significantly fewer recurrences (18% versus 90%) and greater symptom-free survival compared with patients receiving placebo. Patients treated with Kineret were able to wean off of corticosteroids.

- Safety and efficacy of Arcalyst was established in the RHAPSODY trial, a phase III, double-blind, placebo-controlled, randomized withdrawal study of 86 patients with symptomatic pericarditis recurrence. Patients were included if they were presenting with at least their third episode of pericarditis at screening and had been on stable doses of aspirin/NSAIDs, colchicine, and/or glucocorticoids for at least 3 days prior to Arcalyst administration. Patients were excluded if they pericarditis secondary to tuberculosis, post-thoracic blunt trauma, myocarditis, systemic autoimmune diseases, or neoplastic, purulent, or radiation etiologies. The primary efficacy endpoint was time to first adjudicated pericarditis recurrence based on pain, CRP and clinical signs in the event-driven withdrawal period. Of the 61 subjects randomized, 23 (74%) in the placebo arm had a recurrence compared with 2 (7%) in the rilonacept arm who temporarily discontinued treatment for 1 – 3 doses. The median time-to-recurrence on rilonacept could not be estimated because too few events occurred and was 8.6 weeks (95% CI 4.0, 11.7) on placebo with a hazard ratio of 0.04 ( $p < 0.0001$ ). The median time to treatment response was 5 days with a 97% treatment response rate. In addition, patients receiving Arcalyst had a 96% reduction in the risk of a recurrent pericarditis event.
- There is no evidence confirming efficacy of Kineret over Arcalyst for use in recurrent pericarditis, therefore, use of Kineret provides the best value

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Policy History												
#	Date	Change Description										
1.5	Effective Date: 06/08/2023	Annual review of criteria was performed, no changes were made										
1.4	Effective Date: 06/09/2022	Annual review of criteria was performed, no changes were made										
1.3	Effective Date: 09/13/2021	PA added to MAPPO and BCNA <table border="1" data-bbox="483 407 1365 617"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>No</td> </tr> <tr> <td>BCN</td> <td>No</td> </tr> <tr> <td>MAPPO</td> <td>Yes</td> </tr> <tr> <td>BCNA</td> <td>Yes</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	No	MAPPO	Yes	BCNA	Yes
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1.2	Effective Date: 06/10/2021	Updated to add new indication of recurrent pericarditis										
1.1	Effective Date: 02/04/2021	Updated to add new indication of deficiency of IL-1 receptor antagonist										
1.0	Effective Date: 08/13/2020	New policy – previous criteria for Arcalyst was part of the CAPS policy which will be retired.  Updates were made to previous criteria as part of the annual review process. <table border="1" data-bbox="483 936 1365 1146"> <thead> <tr> <th>Line of Business</th> <th>PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td>BCBS</td> <td>No</td> </tr> <tr> <td>BCN</td> <td>No</td> </tr> <tr> <td>MAPPO</td> <td>No</td> </tr> <tr> <td>BCNA</td> <td>No</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	No	MAPPO	No	BCNA	No
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\* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.