Effective Date..... 3/1/2023
Next Review Date..... 3/1/2024

Prior Authorization
Inflammatory Conditions – Arcalyst® (rilonacept subcutaneous injection)

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Product Identifier(s)

Effective 1/1/23 to 2/6/23: 107678

Effective 2/7/23: 12877

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

National Formulary Medical Necessity

Cigna covers rilonacept (Arcalyst®) as medically necessary when the following criteria are met for FDA Indications or Other Uses with Supportive Evidence:

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 individuals 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.

FDA Indication(s)

1. **Cryopyrin-Associated Periodic Syndromes.** Approve for the duration noted if the individual 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 individual meets the following conditions (i and ii):

i. Individual is ≥ 12 years of age; AND
ii. The medication is prescribed by or in consultation with a rheumatologist, geneticist, allergist/immunologist, or dermatologist.

B) Individual is Currently Receiving Arcalyst. Approve for 1 year if the individual meets BOTH of the following (i and ii):
i. Individual has been established on this medication for at least 6 months; AND
Note: An individual who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).
ii. Individual meets at least one of the following (a or b):
a) When assessed by at least one objective measure, individual 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), individual 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 individual meets one of the following (A or B):
A) Initial Therapy. Approve for 6 months if the individual meets all of the following (i, ii, iii, and iv):
i. Individual is ≥ 10 kg (22 pounds); AND
ii. Genetic testing has confirmed a mutation in the *IL1RN* gene; AND
iii. According to the prescriber, individual 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) Individual is Currently Receiving Arcalyst. Approve for 1 year if the individual meets BOTH of the following (i and ii):
i. Individual has been established on this medication for at least 6 months; AND
Note: An individual who has received < 6 months of therapy or who is restarting therapy with this medication is reviewed under criterion A (Initial Therapy).
ii. Individual meets at least one of the following (a or b):
a) When assessed by at least one objective measure, individual 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), individual 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 individual meets one of the following (A or B):
A) Initial Therapy. Approve for 3 months if the individual meets all of the following (i, ii, iii, iv, and v):
i. Individual is ≥ 12 years of age; AND
ii. Individual has recurrent pericarditis; AND
iii. Prior to starting treatment with Arcalyst, the individual had a history of at least three episodes of pericarditis; AND
iv. Individual meets one of the following (a or b):
a) For the current episode, the individual 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) Individual is Currently Receiving Arcalyst. Approve for 1 year if the meets BOTH of the following (i and ii):

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

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

a) When assessed by at least one objective measure, individual 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), individual experienced an improvement in at least one symptom, such as resolution of chest pain or pericarditis pain.

Conditions Not Covered

Rilonacept (Arcalyst®) is considered experimental, investigational or unproven for ANY other use including the following (this list may not be all inclusive):

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).**
Note: This includes requests for cytokine release syndrome associated with COVID-19.

Background

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.

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.

Revision History

Type of Revision	Summary of Changes	Approval Date
Annual Revision	No criteria changes.	01/25/2023

Appendix

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, JIA, PsO, PsA, RA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, nr-axSpA, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, JIA, PsO, PsA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PsO, PsA, RA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, PJIA, PsA, RA
Actemra® (tocilizumab IV infusion, tocilizumab SC injection)	Inhibition of IL-6	SC formulation: PJIA, RA, SJIA
		IV formulation: PJIA, RA, SJIA
Kevzara® (sarilumab SC injection)	Inhibition of IL-6	RA
Orencia® (abatacept IV infusion, abatacept SC injection)	T-cell costimulation modulator	SC formulation: JIA, PsA, RA
		IV formulation: JIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Kineret® (anakinra SC injection)	Inhibition of IL-1	JIA^, RA
Stelara® (ustekinumab SC injection, ustekinumab IV infusion)	Inhibition of IL-12/23	SC formulation: CD, PsO, PsA, UC
		IV formulation: CD, UC
Siliq™ (brodalumab SC injection)	Inhibition of IL-17	PsO
Cosentyx® (secukinumab SC injection)	Inhibition of IL-17A	AS, ERA, nr-axSpA, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, nr-axSpA, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi® (risankizumab-rzaa SC injection)	Inhibition of IL-23	PsA, PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC

* 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.