Pharmacy Benefit Coverage Criteria

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Coverage Policy Number P0007

Rilonacept

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Related Coverage Resources

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

Coverage Policy

Rilonacept (Arcalyst™) is considered medically necessary when ONE of the following are met:

- **Cryopyrin-Associated Periodic Syndromes (CAPS) and BOTH of the following:**
  Note: This includes Familial Cold autoinflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS), Neonatal Onset Multisystem Inflammatory Disease (NOMID), Chronic Infantile Neurological Cutaneous and Articular (CINCA) Syndrome
  - Age 12 years of age and older
  - Arcalyst is prescribed by or in consultation with a rheumatologist, geneticist, allergist/immunologist, or dermatologist

- **Deficiency of Interleukin-1 Receptor Antagonist (DIRA) and ALL of the following:**
  - Individual is greater than or equal to 10 kg (22 pounds)
  - Genetic testing has confirmed a mutation in the *IL1RN* gene
  - According to the prescriber, patient has demonstrated a clinical benefit with Kineret (anakinra subcutaneous injection)
    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.
  - The medication is prescribed by or in consultation with a rheumatologist, geneticist, dermatologist, or a physician specializing in the treatment of autoinflammatory disorders.

- **Pericarditis and ALL of the following**
    - Individual is 12 years of age or older
    - Individual has recurrent pericarditis
    - Prior to starting treatment with Acralyst, the individual has a history of at least three episodes of pericarditits
    - Individual meets ONE of the following:
        - o For the current episode, individual has acute signs and symptoms of pericarditis despite standard treatment
        - o Standard treatment is contraindicated

        Note: Standard treatments for pericarditis include nonsteroidal anti-inflammatory drug(s) [NSAIDs], colchicine, and/or systemic corticosteroids.
    - Prescribed by or in consultation with a cardiologist or rheumatologist

Rilonacept (Arcalyst) is considered medically necessary for continued use when the following is met:
- Documentation of positive clinical response to rilonacept

For CAPS and DIRA, initial and reauthorization is up to 12 months unless otherwise stated.
For pericarditis, initial authorization is up to 3 months. Reauthorization is up to 12 months.

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 as applicable.

Rilonacept (Arcalyst) is considered experimental, investigational or unproven for ANY other use including the following:
- Adult Onset Still's Disease
- Gout
- Gouty arthritis
- Juvenile idiopathic arthritis
- Schnitzler Syndrome
- Type 1 diabetes
- Concurrent biologic therapy (Arcalyst should not be administered in combination with another biologic agent for an inflammatory condition)
- COVID-19 (Coronavirus Disease 2019), including cytokine release syndrome associated with COVID-19

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

Background

OVERVIEW
Arcalyst, an interleukin-1 (IL-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 symptoms scores were improved with Arcalyst through Week 6 and were maintained through Week 15. In 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, there were a mean of 4.4 episodes per year (including the qualifying event). All

patients who enrolled in the study were symptomatic despite treatment with standard treatment (e.g., nonsteroidal anti-inflammatory drugs, 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).[9] 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.

Experimental, Investigational, Unproven Uses

Arcalyst has been evaluated for use in adult onset Still's disease[6], gout and gouty arthritis[4,5], juvenile idiopathic arthritis[5], Schnitzler syndrome[7], type 1 diabetes[5]. At this time, however, there is insufficient published data in terms of safety and efficacy to support the use of Arcalyst in these conditions.

Arcalyst should not be administered in combination with another biologic agent for an inflammatory condition (see table 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.

	Mechanism of Action	Examples of Inflammatory Indications*
Biologics		
Adalimumab SC Products (Humira®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Cimzia® (certolizumab pegol SC injection)	Inhibition of TNF	AS, CD, PsO, PsA, RA
Etanercept SC Products (Enbrel®, biosimilars)	Inhibition of TNF	AS, PJIA, PsO, PsA, RA, SJIA
Infliximab IV Products (Remicade®, biosimilars)	Inhibition of TNF	AS, CD, PJIA, PsO, PsA, RA, SJIA, UC
Simponi®, Simponi® Aria™ (golimumab SC injection, golimumab IV infusion)	Inhibition of TNF	SC formulation: AS, PsA, RA, UC
		IV formulation: AS, 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: PJIA, PSA, RA
		IV formulation: PJIA, PsA, RA
Rituximab IV Products (Rituxan®, biosimilars)	CD20-directed cytolytic antibody	RA
Ilaris (canakinumab SC injection**)**	Inhibition of IL-1β	SJIA
Kineret® (anakinra SC injection)	Inhibition of IL-1	RA, SJIA^
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, PsO, PsA
Taltz® (ixekizumab SC injection)	Inhibition of IL-17A	AS, PsO, PsA
Ilumya™ (tildrakizumab-asmn SC injection)	Inhibition of IL-23	PsO
Skyrizi™ (risankizumab-rzza SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO

	Mechanism of Action	Examples of Inflammatory Indications*
Entyvio™ (vedolizumab IV infusion)	Integrin receptor antagonist	CD, UC
Targeted Synthetic DMARDs		
Otezla® (apremilast tablets)	Inhibition of PDE4	PsO, PsA
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways	RA
Rinvoq® (upadacitinib extended-release tablets)	Inhibition of the JAK pathways	RA
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways	RA, PsA, 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; IV – Intravenous, IL – Interleukin; PDE4 – Phosphodiesterase 4; JAK – Janus kinase; AS – Ankylosing spondlylitis; CD – Crohn's disease; PJIA – Polyarticular juvenile idiopathic arthritis; PsO – Plaque psoriasis; PsA – Psoriatic arthritis; RA – Rheumatoid arthritis; SJIA – Systemic juvenile idiopathic arthritis; UC – Ulcerative colitis; ^ Off-label use of SJIA supported in guidelines.

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