VENTURA COUNTY
HEALTH CARE PLAN

PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Arcalyst® (rilonacept for subcutaneous injection – Regeneron Pharmaceuticals)

TAC APPROVAL DATE: 11/07/2018

OVERVIEW

Arcalyst is an interleukin-1 (IL-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 aged 12 years and older.[1] Arcalyst, also known is a recombinant dimeric fusion protein that blocks IL-1β signaling and to a lesser extent also binds IL-1α and IL-1 receptor antagonist (IL-1ra). In adults ≥ 18 years of age, Arcalyst is initiated with a loading dose of 320 mg delivered as two subcutaneous (SC) injections of 160 mg on the same day at two separate sites. Dosing is continued with 160 mg once weekly as a single injection. In adolescents aged 12 to 17 years, therapy is initiated with a loading dose of 4.4 mg/kg, up to a maximum of 320 mg, delivered as one or two SC injections with a maximum single-injection volume of 2 mL. If the initial dose is two injections, then patients should be given Arcalyst on the same day at two separate sites. In adolescents, dosing is continued with 2.2 mg/kg, up to a maximum of 160 mg, once weekly as a single injection.

Disease Overview

CAPS is a rare inherited inflammatory disease associated with overproduction of IL-1. CAPS encompasses three rare genetic syndromes. FCAS, MWS, and neonatal onset multisystem inflammatory disorder (NOMID) or chronic infantile neurological cutaneous and articular syndrome (CINCA) are thought to be one condition along a spectrum of disease severity.[2-3] FCAS is the mildest phenotype and NOMID is the most severe. There are no reliable prevalence statistics for CAPS, but the estimated number of persons with CAPS in the US is 200 to 500. These three disorders may be associated with mutations in the *CIAS-1* gene and have autosomal dominant inheritance. Mutations in the *CIAS-1* gene, which encodes a protein (cryopyrin), cause excess release of IL-1β and an inflammatory response. IL-1 cytokine signaling is important in the pathogenesis of CAPS. These autoinflammatory syndromes are caused by episodes of inflammation and are distinct from autoimmune disorders. The inflammatory symptoms in these patients include atypical urticaria, rash that is worse in the evening, fever, chills, fatigue, arthralgia, and conjunctival erythema. Exacerbations or flares can be triggered by exposure to cold, stress, exercise, or other stimuli. Patients with NOMID may have sensorineural hearing impairment, increased intracranial pressure, and joint abnormalities. One-fourth of patients with MWS may develop systemic amyloid A (AA) amyloidosis which usually presents with renal impairment and nephrotic syndrome; amyloidosis is less common in the other forms of CAPS.

POLICY STATEMENT

Prior authorization is recommended for prescription benefit coverage of Arcalyst. 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. 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Arcalyst is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Cryopyrin-Associated Periodic Syndromes (CAPS) (including Familial Cold Autoinflammatory Syndrome [FCAS], Muckle-Wells Syndrome [MWS], and Neonatal Onset Multisystem Inflammatory Disease [NOMID] or Chronic Infantile Neurological Cutaneous and Articular [CINCA] Syndrome).** 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 the following conditions (i and ii):
     - **i.** The patient is ≥ 12 years of age; AND
     - **ii.** Arcalyst is prescribed by or in consultation with a rheumatologist, geneticist, allergist/immunologist, or dermatologist.
   - **B)** Patient is Currently Receiving Arcalyst. Approve for 3 years if the patient has had a response, as determined by the prescriber.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Arcalyst has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. Rationale for non-coverage for these specific conditions is provided below. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval.)

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 TNF blocking agents. An increased incidence of serious infections has been associated with another IL-1 blocker (Kineret) when given in combination with TNF antagonists.

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

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3. Ozen S, Hoffman HM, Frenkel J, et al. Familial Mediterranean Fever (FMF) and beyond: a new horizon. Fourth International Congress on the Systemic Autoinflammatory Diseases held in Bethesda, USA, 6-10 November 2005. *Ann Rheum Dis.* 2006;65:961-964.
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5. Hoffman HM, Throne ML, Amar NJ, et al. Efficacy and safety of rilonacept (interleukin-1 Trap) in patients with cryopyrin-associated periodic syndromes: results from two sequential placebo-controlled studies. *Arthritis Rheum.* 2008;58:2443-2452.
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7. Kuemmerle-Deschner JB, Hachulla E, Cartwright R, et al. Two-year results from an open-label, multicentre, phase III study evaluating the safety and efficacy of canakinumab in patients with cryopyrin-associated periodic syndrome across different severity phenotypes. *Ann Rheum Dis*. 2011;70(12):2095-2102.
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12. Ringold S, Weiss PF, Beukelman T, et al. 2013 update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: recommendations for the medical therapy of children with systemic juvenile idiopathic arthritis and tuberculosis screening among children receiving biologic medications. *Arthritis Rheum*. 2013;65(10):2499-2512.
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OTHER REFERENCES UTILIZED

- Goldbach-Mansky R, Shroff SD, Wilson M, et al. A pilot study to evaluate the safety and efficacy of the long-acting interleukin-1 inhibitor rilonacept (interleukin-1 Trap) in patients with familial cold autoinflammatory syndrome. *Arthritis Rheum*. 2008;58:2432-2442.
- Terkeltaub R, Sundy JS, Schumacher HR, et al. The interleukin 1 inhibitor rilonacept in treatment of chronic gouty arthritis: results of a placebo-controlled, monosequence crossover, non-randomised, single-blind pilot study. *Ann Rheum Dis*. 2009;68(10):1613-1617.
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- Koné-Paut I, Galeotti C. Current treatment recommendations and considerations for cryopyrin-associated periodic syndrome. *Expert Rev Clin Immunol*. 2015;11(10):1083-1092.

HISTORY

Type of Revision	Summary of Changes*	TAC Approval Date
Annual revision	Add allergist/immunologist to the list of prescribers who may be involved in prescribing Arcalyst for CAPS.	09/30/2015
Annual revision	Gout is removed from the Conditions Not Recommended for Approval and is no longer addressed in the policy.	10/05/2016
Annual revision	Remove Familial Mediterranean Fever and Systemic Juvenile Idiopathic Arthritis from the Conditions Not Recommended for Coverage (not needed).	10/11/2017
Annual revision	No criteria changes.	11/07/2018

* For a further summary of criteria changes, refer to respective TAC minutes available at: http://esidepartments/sites/Dep043/Committees/TAC/Forms/AllItems.aspx; TAC – Therapeutic Assessment Committee; CAPS – Cryopyrin-associated periodic syndrome.

APPENDIX

Brand (generic name)	Mechanism of Action
Cimzia® (certolizumab pegol for SC injection)	Inhibition of TNF
Enbrel® (etanercept for SC injection)	Inhibition of TNF
Erelzi™ (etanercept-szzs for SC injection)	Inhibition of TNF
Humira® (adalimumab for SC injection)	Inhibition of TNF
Amjevita® (adalimumab-atto for SC injection)	Inhibition of TNF
Cyltezo® (adalimumab-adbm for SC injection)	Inhibition of TNF
Simponi® (golimumab for SC injection)	Inhibition of TNF
Simponi® Aria™ (golimumab for IV infusion)	Inhibition of TNF
Remicade® (infliximab for IV infusion)	Inhibition of TNF
Inflectra™ (infliximab-dyyb for IV infusion)	Inhibition of TNF
Renflexis® (infliximab-abda for IV infusion)	Inhibition of TNF
Actemra® (tocilizumab for IV infusion)	Inhibition of IL-6
Actemra® (tocilizumab for SC injection)	Inhibition of IL-6
Kevzara® (sarilumab for SC injection)	Inhibition of IL-6
Orencia® (abatacept for IV infusion)	T-cell costimulation modulator
Orencia® (abatacept for SC injection)	T-cell costimulation modulator
Rituxan® (rituximab for IV infusion)	CD20-directed cytolytic antibody
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1
Stelara® (ustekinumab for SC injection)	Inhibition of IL-12/23
Stelara® (ustekinumab for IV infusion)	Inhibition of IL-12/23
Siliq™ (brodalumab SC injection)	Inhibition of IL-17
Cosentyx™ (secukinumab for SC injection)	Inhibition of IL-17A
Taltz® (ixekizumab for SC injection)	Inhibition of IL-17A
Ilumya™ (tildrakizumab-asmn for SC injection)	Inhibition of IL-23
Tremfya™ (guselkumab for SC injection)	Inhibition of IL-23
Otezla® (apremilast tablets)	Inhibition of PDE4
Olumiant® (baricitinib tablets)	Inhibition of the JAK pathways
Xeljanz®, Xeljanz XR (tofacitinib tablets, tofacitinib extended-release tablets)	Inhibition of the JAK pathways
Kineret® (anakinra for subcutaneous SC injection)	Inhibition of IL-1
Arcalyst® (rilonacept SC injection)	Inhibition of IL-1
Ilaris® (canakinumab SC injection)	Inhibition of IL-1

SC – Subcutaneous; TNF – Tumor necrosis factor; IV – Intravenous, IL – Interleukin;PDE4 – Phosphodiesterase 4; JAK – Janus kinase.