PRIOR AUTHORIZATION POLICY

POLICY: Inflammatory Conditions – Arcalyst Prior Authorization Policy
- Arcalyst® (rilonacept subcutaneous injection – Regeneron)

REVIEW DATE: 01/20/2021; selected revision 04/07/2021 and 08/11/2021

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.

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.

All reviews for use of Arcalyst for COVID-19 and/or cytokine release syndrome associated with COVID-19 will be forwarded to the Medical Director.

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.** Approve for the duration noted if the patient 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 3 months if the patient meets the following conditions (i and ii):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** The medication 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.

2. **Deficiency of Interleukin-1 Receptor Antagonist**. Approve for the duration noted if the patient meets one of the following (A or B):
   - **A)** Initial Therapy. Approve for 6 months if the patient meets all of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 10 kg (22 pounds); AND
     - **ii.** Genetic testing has confirmed a mutation in the *IL1RN* gene; AND
     - **iii.** According to the prescriber, patient 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)** Patient is Currently Receiving Arcalyst. Approve for 3 years if the patient has responded to therapy, as determined by the prescriber.
     Note: Examples include sustained remission; continued resolution of fever, skin rash, and bone pain; normalized acute phase reactants.

3. **Pericarditis.** 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 all of the following (i, ii, iii, iv, and v):
     - **i.** Patient is ≥ 12 years of age; AND
     - **ii.** Patient has recurrent pericarditis; AND
     - **iii.** Prior to starting treatment with Arcalyst, the patient has a history of at least three episodes of pericarditis; AND
     - **iv.** Patient meets one of the following (a or b):
       - **a)** For the current episode, the patient 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) Patient is Currently Receiving Arcalyst. Approve for 1 year if the patient has a clinical response, as determined by the prescriber.
Note: Examples of clinical response include the absence of symptoms of pericarditis (e.g., absence of chest pain with normalization of inflammatory biomarkers such as erythrocyte sedimentation rate and/or C-reactive protein), continued resolution of fever and bone pain.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Arcalyst is not recommended in the following situations:

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).** Forward all requests to the Medical Director.
Note: This includes requests for cytokine release syndrome associated with COVID-19.

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

REFERENCES

1. Arcalyst® for injection [prescribing information]. Tarrytown, NY: Regeneron Pharmaceuticals; 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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	11/06/2019
Selected Revision	**COVID-19:** This indication (including use in cytokine release syndrome associated with COVID-19) was added to the policy as a Condition Not Recommended for Coverage. All reviews are directed to the Medical Director.	04/01/2020
Annual Revision	No criteria changes.	11/18/2020
Early Annual Revision	**Deficiency of Interleukin-1 Receptor Antagonist:** Criteria for this newly approved condition were added to the policy. For an initial 6-month approval, the patient must weigh ≥ 22 kg, genetic testing must have confirmed a mutation in the *IL1RN* gene, and the patient must have tried Kineret. Additionally, Arcalyst must be prescribed by or in consultation with a specialist. For a patient currently taking Arcalyst, a 3-year approval is authorized in the patient has responded to therapy.	01/20/2021
Selected Revision	**Pericarditis:** This newly approved indication was added to the policy. Criteria approve for 3 months of initial therapy if the patient is ≥ 12 years of age with recurrent pericarditis, if the patient is taking standard therapies, unless contraindicated, and if prescribed by or in consultation with a cardiologist or rheumatologist. Prior to starting Arcalyst, there is also a requirement that the patient has at least three episodes of pericarditis in the previous year. Criteria approve for 1 year for a patient currently taking Arcalyst if the patient had a clinical response.	04/07/2021
Selected Revision	**Pericarditis:** The requirement that the patient has a history of at least three episodes of pericarditis prior to starting Arcalyst was changed to remove the requirement that these episodes were in the past year.	08/11/2021

APPENDIX

	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-rzaa SC injection)	Inhibition of IL-23	PsO
Tremfya™ (guselkumab SC injection)	Inhibition of IL-23	PsO
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; AS – Ankylosing spondylitis; 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; IV – Intravenous; IL – Interleukin; ^ Off-label use of SJIA supported in guidelines; PDE4 – Phosphodiesterase 4; JAK – Janus kinase.

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Aspirus Health Plan, Inc.
PO Box 1062
Minneapolis, MN 55440
Phone: 1.866.631.5404 (TTY: 711)
Fax: 763.847.4010
Email: customerservice@aspirushealthplan.com

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U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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Albanian: KUJDES: Nëse flitni shqip, për ju ka në dispozicion shërbime të asistencës gjuhësore, pa pagesë.Telefononi në 1.866.631.5404 (TTY: 711).

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Hmong: LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 1.866.631.5404 (TTY: 711).

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Lao: ໂປດຊາບ: ຖ້າວ່າ ທ່ານເວົ້າພາສາ ລາວ, ການບໍລິການຊ່ວຍເຫຼືອດ້ານພາສາ,ໂດຍບໍ່ເສັ້ງຄ່າ, ແມ່ນມີພ້ອມໃຫ້ທ່ານ. ໂທຣ 1.866.631.5404 (TTY:711).