Medical Policy:

Arcalyst® (rilonacept) Subcutaneous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.132	February 18, 2025	July 15, 2019

The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

Definitions

Arcalyst is a targeted inhibitor of interleukin-1 (IL-1), the key driver of inflammation in cryopyrin-associated periodic syndromes (CAPS). Rilonacept acts as a decoy receptor that binds IL-1 beta and the blocks IL-1 beta signaling, thereby preventing its interaction with cell surface receptors. It also binds IL-1 alpha and IL-1 receptor antagonist with reduced affinity

Length of Authorization

Coverage will be provided for 6 months and may be renewed.

Dosing Limits

Max Units (per dose and over time) [HCPCS Unit]:

Cryopyrin-Associated Periodic Syndromes (CAPS)/Recurrent Pericarditis (RP)

- Loading Dose: 320 billable units on Day 1
- Maintenance Dose: 160 billable units every 7 days

Deficiency of Interleukin-1 Receptor Antagonist (DIRA)

• 320 billable units every 7 days

Guideline

I. INITIAL APPROVAL CRITERIA

Arcalyst *may be considered medically necessary if the below condition is met* ***AND*** *use is consistent with the medical necessity criteria that follows:*

1. Cryopyrin-Associated Periodic Syndromes

A. Patient has documented baseline serum levels of inflammatory proteins (C-Reactive Protein [CRP] and/or Serum Amyloid A [SAA], etc.); **AND**

B. Patient has documented laboratory evidence of a genetic mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1), also known as NLRP3; **AND**

i. Documented diagnosis of Familial Cold Autoinflammatory Syndrome (FCAS); **OR**

ii. Documented diagnosis of Muckle-Wells Syndrome (MWS); **AND**

C. Prescribed by, or in consultation with, a rheumatologist, geneticist, allergist/immunologist, or dermatologist; **AND**

D. Age ≥ 12 years; **AND**

E. Used as a single agent; **AND**

F. Dose does not exceed a loading dose of 320 mg (as two injections) and once weekly dosing of 160 mg (as a single injection); **AND**

G. Patient has **TWO** or more of any of the CAPS-typical symptoms:

- urticaria-like rash
- cold-triggered episodes
- sensorineural hearing loss
- musculoskeletal symptoms
- chronic aseptic meningitis
- skeletal abnormalities

2. Deficiency of Interleukin-1 Receptor Antagonist (DIRA)

A. Patient weighs at least 10 kg; **AND**

B. Patient has a confirmed diagnosis of DIRA as evidenced by a mutation in the *IL1RN* gene; **AND**

C. Used as maintenance of remission in patients who have previously experienced clinical benefit from anakinra therapy for the treatment of DIRA

3. Recurrent Pericarditis (RP)

A. Patient is at least 12 years of age; **AND**

B. Used for the treatment of recurrent pericarditis and/or reducing the recurrence of disease; **AND**

C. Patient has documented baseline serum levels of inflammatory proteins (C-Reactive Protein [CRP], etc.); **AND**

D. Patient has failed standard therapy (e.g., NSAID, colchicine, corticosteroids, etc.)

II. RENEWAL CRITERIA

1. Patient continues to meet INITIAL APPROVAL CRITERIA; **AND**

2. Absence of unacceptable toxicity from the drug. *Examples of unacceptable toxicity include: severe hypersensitivity reactions, serious infections (including but not limited to tuberculosis), lipid profile changes, etc*.; **AND**
   A. **Cryopyrin-Associated Periodic Syndromes**: Disease response as indicated by improvement in patient's symptoms from baseline **AND** improvement in serum levels of inflammatory proteins (e.g. CRP and/or SAA, etc.) from baseline
   B. **Deficiency of Interleukin-1 Receptor Antagonist (DIRA):** Disease response as indicated by improvement in patient's symptoms (e.g., fever, skin rash, bone pain), inflammatory markers (e.g., CRP, ESR), and/or radiological evidence of active bone lesions compared to baseline
   C. **Recurrent Pericarditis (RP):** Disease response as indicated by improvement in patient's symptoms (e.g., pericarditis pain, etc.), inflammatory markers (e.g., CRP, etc.), and/or decreased rate of recurrence of disease compared to baseline

Limitations/Exclusions

1. Patient is not on concurrent therapy with other IL-1 blocking agents (e.g., canakinumab, anakinra*, etc.) *[*Note: For DIRA, anakinra must be discontinued 24 hours prior to starting Arcalyst]*; **AND**
2. Patient is not on concurrent treatment with another TNF inhibitor, biologic response modifier or other non-biologic immunomodulating agent (e.g., apremilast, tofacitinib, baricitinib, upadacitinib, abrocitinib, deucravacitinib, etc.) **AND**
3. Patient has been evaluated and screened for the presence of latent tuberculosis (TB) infection prior to initiating treatment and will receive ongoing monitoring for the presence of TB during treatment; **AND**
4. Patient does not have an active infection, including clinically important localized infections; **AND**
5. Will not be administered concurrently with live vaccines **AND**
6. Patient is up to date with all vaccinations, in accordance with current vaccination guidelines, prior to initiating therapy

Dosage/Administration

Indication	Dose
Cryopyrin-Associated Periodic Syndromes & Recurrent Pericarditis (Adult patients 18 and older)	Initiate treatment with a loading dose of 320 mg delivered as two, 2-mL, subcutaneous injections of 160 mg on the same day at two different sites. Continue dosing with a once-weekly injection of 160 mg administered as a single, 2-mL, subcutaneous injection
Cryopyrin-Associated Periodic Syndromes & Recurrent Pericarditis (Pediatric patients aged 12 to 17)	Initiate treatment with a loading dose of 4.4 mg/kg, up to a maximum of 320 mg, delivered as one or two subcutaneous injections with a maximum single-injection volume of 2-mL. Continue dosing with a once-weekly injection of 2.2 mg/kg, up to a maximum of 160 mg, administered as a single subcutaneous injection, up to 2-mL. If the initial dose is given as two injections, they should be given on the same day at two different sites
Deficiency of Interleukin-1 Receptor Antagonist (Adult patients 18 and older)	The recommended dose is 320 mg once weekly delivered as two, 2-mL, subcutaneous injections of 160 mg on the same day at two different sites. **NOTE: Treatment with anakinra will be stopped 24 hours before initiation of Arcalyst*
Deficiency of Interleukin-1 Receptor Antagonist (Pediatric patients < 18 years of age and weighing at least 10 kg)	The recommended dose is 4.4 mg/kg (up to a maximum of 320 mg) once weekly delivered as one or two, subcutaneous injections with a maximum single-injection volume of 2 mL (160 mg). If the dose is given as two injections, they should be given on the same day at two different sites. **NOTE: Treatment with anakinra will be stopped 24 hours before initiation of Arcalyst*

Applicable Procedure Codes

Code	Description
J2793	Injection, rilonacept, 1 mg, 1 billable unit = 1 mg

Applicable NDCs

Code	Description
73604-0914-xx	Arcalyst single use vial; 220 mg (each reconstituted vial delivers 160 mg)

ICD-10 Diagnoses

Code	Description
E85.0	Non-neuropathic heredofamilial amyloidosis
I24.1	Dressler's Syndrome
L50.2	Urticaria due to cold and heat [familial cold autoinflammatory syndrome (FCAS)]
M04.2	Cryopyrin-associated periodic syndromes
M04.8	Other autoinflammatory syndromes

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	2/18/2025	Annual Review: Addition to renewal criteria: Patient has been evaluated and screened for the presence of latent tuberculosis (TB) infection prior to initiating treatment and will receive ongoing monitoring for the presence of TB during treatment; **AND** Patient does not have an active infection, including clinically important localized infections; **AND** Will not be administered concurrently with live vaccines **AND** Patient is up to date with all vaccinations, in accordance with current vaccination guidelines, prior to initiating therapy Addition to initial criteria for (CAPS) Used as a single agent
EmblemHealth & ConnectiCare	4/9/2024	Annual Review: Added dosing limits, updated dosing chart, added limitations/exclusions. Initial Criteria: Cryopyrin-Associated Periodic Syndromes: removed the following statement to clarify: "Diagnosis of Familial Cold Autoinflammatory Syndrome (FCAS) or Muckle-Wells Syndrome (MWS); AND" Clarified as:"Patient has documented baseline serum levels of inflammatory proteins (C-Reactive Protein [CRP] and/or Serum Amyloid A [SAA], etc.); AND Patient has documented laboratory evidence of a genetic mutation in the Cold-Induced Auto-inflammatory Syndrome 1 (CIAS1), also known as NLRP3; AND Documented diagnosis of Familial Cold Autoinflammatory Syndrome (FCAS); OR" Documented diagnosis of Muckle-Wells Syndrome (MWS); AND Updated prescribers to include: "geneticist, allergist/immunologist, or dermatologist; AND" Renewal Criteria: Removed the following statement to clarify: " Member is responding positively to therapy." Added:"Absence of unacceptable toxicity from the drug. *Examples of unacceptable toxicity include: severe hypersensitivity reactions, serious infections (including but not limited to tuberculosis), lipid profile changes, etc*.; AND Cryopyrin-Associated Periodic Syndromes: Disease response as indicated by improvement in patient's symptoms from baseline AND improvement in serum levels of inflammatory proteins (e.g. CRP and/or SAA, etc.) from baseline Deficiency

		of Interleukin-1 Receptor Antagonist (DIRA): Disease response as indicated by improvement in patient's symptoms (e.g., fever, skin rash, bone pain), inflammatory markers (e.g., CRP, ESR), and/or radiological evidence of active bone lesions compared to baseline Recurrent Pericarditis (RP): Disease response as indicated by improvement in patient's symptoms (e.g., pericarditis pain, etc.), inflammatory markers (e.g., CRP, etc.), and/or decreased rate of recurrence of disease compared to baseline"
EmblemHealth & ConnectiCare	8/2/2023	Annual Review: Cryopyrin-Associated Periodic Syndromes :Initial Criteria: Added "Patient has two or more of any of the CAPS-typical symptoms: – urticaria-like rash – cold-triggered episodes – sensorineural hearing loss – musculoskeletal symptoms – chronic aseptic meningitis – skeletal abnormalities" Added Deficiency of Interleukin-1 Receptor Antagonist (DIRA) Indication and Criteria Added Recurrent Pericarditis (RP) indication and criteria Removed NDC 61755-001-xx, added 73604-0914-xx Added ICD-10 Codes: E85.0, I24.1, M04.2, and M04.8 Updated dosing chart
EmblemHealth & ConnectiCare	3/23/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	7/15/2019	Annual review – no changes

References

1. Product Information: ARCALYST® subcutaneous injection, rilonacept subcutaneous injection. Regeneron Pharmaceuticals, Inc. (per Manufacturer), Tarrytown, NY, 2014.
2. Hoffman HM, Rosengren S, Boyle DL, et al. Prevention of cold-associated acute inflammation in familial cold autoinflammatory syndrome by interleukin-1 receptor antagonist. Lancet. 2004;364(9447):1779-1785.
3. Shinkai K, McCalmont TH, Leslie KS. Cryopyrin-associated periodic syndromes and autoinflammation. Clin Exp Dermatol. 2008;33(1):1-9.