

## **Clinical Policy: Riloncept (Arcalyst)**

Reference Number: CP.PHAR.266

Effective Date: 11.16.16

Last Review Date: 08.21

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Riloncept (Arcalyst<sup>®</sup>) is an interleukin-1 blocker.

### **FDA Approved Indication(s)**

Arcalyst is indicated for:

- Treatment of cryopyrin-associated periodic syndromes (CAPS), including familial cold autoinflammatory syndrome (FCAS) and Muckle-Wells syndrome (MWS) in adults and children 12 and older.
- Maintenance of remission of deficiency of interleukin-1 receptor antagonist (DIRA) in adults and pediatric patients weighing at least 10 kg.
- Treatment of recurrent pericarditis (RP) and reduction in risk of recurrence in adults and pediatric patients 12 years and older.

### **Policy/Criteria**

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Arcalyst is **medically necessary** when the following criteria are met:

#### **I. Initial Approval Criteria**

##### **A. Cryopyrin-Associated Periodic Syndromes (must meet all):**

1. Diagnosis of FCAS or MWS;
2. Prescribed by or in consultation with a rheumatologist;
3. Age  $\geq$  12 years;
4. Documentation of one of the following (a or b):
  - a. For FCAS, classic signs and symptoms (e.g., recurrent, intermittent fever and rash often exacerbated by exposure to generalized cool ambient temperature) AND functional impairment limiting activities of daily living;
  - b. For MWS, classic signs and symptoms (e.g., chronic fever and rash of waxing and waning intensity, sometimes exacerbated with exposure to generalized cool ambient temperature) AND functional impairment limiting activities of daily living;
5. Dose does not exceed a loading dose of 320 mg (as two injections) and once weekly dosing of 160 mg (as a single injection).

##### **Approval duration:**

**Medicaid/HIM – 6 months**

**Commercial** – 6 months or to the member’s renewal date, whichever is longer

**B. Deficiency of Interleukin-1 Receptor Antagonist (must meet all):**

1. Diagnosis of DIRA confirmed by presence of loss-of-function *ILRN* mutations;
2. Prescribed by or in consultation with a rheumatologist;
3. Weight  $\geq$  10 kg;
4. Member is in remission and has been stable for  $\geq$  6 months;
5. Dose does not exceed 4.4 mg/kg (up to 320 mg) once weekly.

**Approval duration:**

**Medicaid/HIM** – 6 months

**Commercial** – 6 months or to the member’s renewal date, whichever is longer

**C. Recurrent Pericarditis (must meet all):**

1. Diagnosis of RP with pericarditis that recurs after a symptom-free interval of  $\geq$  4 weeks after an acute pericarditis episode;
2. Prescribed by or in consultation with a cardiologist or rheumatologist;
3. Age  $\geq$  12 years;
4. Member meets one of the following for the recurrent episode (a or b):
  - a. Failure of colchicine in combination with an NSAID (e.g., aspirin, ibuprofen, indomethacin) at up to maximally indicated doses;
  - b. Member has intolerance or contraindication to NSAIDs, and has had a failure of colchicine in combination with a glucocorticoid (e.g., prednisone) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed a loading dose of 320 mg (as two injections) and once weekly dosing of 160 mg (as a single injection).

**Approval duration:**

**Medicaid/HIM** – 6 months

**Commercial** – 6 months or to the member’s renewal date, whichever is longer

**D. Other diagnoses/indications**

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy**

**A. All Indications in Section I (must meet all):**

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
  - a. For CAPS or RP: 160 mg (as a single injection) once weekly;
  - b. For DIRA: 4.4 mg/kg (up to 320 mg) once weekly.

**Approval duration:**

**Medicaid/HIM** – 12 months

**Commercial** – 6 months or to the member’s renewal date, whichever is longer

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

**Approval duration: Duration of request or 6 months (whichever is less); or**

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
- B. Combination use of biological disease-modifying antirheumatic drugs (DMARDs), including any tumor necrosis factor (TNF) antagonists [Cimzia, Enbrel, Simponi, Avsola, Inflectra, Remicade, Renflexis], interleukin agents [Arcalyst (IL-1 blocker), Ilaris (IL-1 blocker), Kineret (IL-1RA), Actemra (IL-6RA), Kevzara (IL-6RA), Stelara (IL-12/23 inhibitor), Cosentyx (IL-17A inhibitor), Taltz (IL-17A inhibitor), Siliq (IL-17RA), Ilumya (IL-23 inhibitor), Skyrizi (IL-23 inhibitor), Tremfya (IL-23 inhibitor)], janus kinase inhibitors (JAKi) [Xeljanz/Xeljanz XR Rinvoq], anti-CD20 monoclonal antibodies [Rituxan, Riabni, Ruxience, Truxima, and Rituxan Hycela], selective co-stimulation modulators [Orencia], or integrin receptor antagonists [Entyvio] because of the possibility of increased immunosuppression, neutropenia and increased risk of infection.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

CAPS: cryopyrin-associated periodic syndromes

DIRA: deficiency of interleukin-1 receptor antagonist

FCAS: familial cold autoinflammatory syndrome

FDA: Food and Drug Administration

MWS: Muckle-Wells syndrome

RP: recurrent pericarditis

*Appendix B: Therapeutic Alternatives*

*This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.*

<b>Drug Name</b>	<b>Dosing Regimen</b>	<b>Dose Limit/ Maximum Dose</b>
aspirin*	<b>RP:</b> 650 – 975 mg PO TID-QID	3,900 mg/day
ibuprofen* (Advil, Motrin)	<b>RP:</b> 400 – 800 mg PO TID	2,400 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
indomethacin* (Indocin)	<b>RP:</b> 50 mg PO TID	150 mg/day
colchicine*	<b>RP:</b> 0.5 mg or 0.6 mg PO BID	1.2 mg/day
prednisone*	<b>RP:</b> 0.25 – 0.5 mg/kg/day	0.5 mg/kg/day

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

\*Off-label

#### Appendix C: Contraindications/Boxed Warnings

None reported

#### Appendix D: General Information

- Three related conditions make up the broader disease known as CAPS: FCAS, MWS, and neonatal-onset multisystem inflammatory disease (NOMID), also known as chronic infantile neurologic cutaneous articular syndrome (CINCA). Arcalyst is not FDA-approved for use in patients with NOMID/CINCA.
- DIRA patients are homozygous or compound heterozygous for loss-of-function mutations in *IL1RN*, encoding IL-1Ra. Most mutations are nonsense or frameshift mutations that lead to either no expression of protein or expression of nonfunctional protein. Examples of disease-causing mutations in *IL1RN* identified include: 4 nonsense mutations, 1 in-frame deletion, 3 frameshift deletions, and a 22-kb and a genomic 175-kb deletion on chromosome 2.
- Concomitant administration of Arcalyst with tumor necrosis factor (TNF) inhibitors (e.g., Enbrel, Humira, or Remicade) and interleukin-1 blocking agents (e.g., Kineret) is not recommended because this may increase the risk of serious infections.
- Examples of positive response to therapy in CAPS include reduction/normalization of: C-reactive protein levels, serum amyloid A levels, flare frequency, or severity and duration of symptoms (e.g., joint pain, rash, fever/chills, eye pain, fatigue).
- Do not initiate treatment with Arcalyst in patients with active or chronic infections.

## V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CAPS (FCAS, MWS), RP	Age ≥ 18 years: 320 mg SC loading dose followed by 160 mg SC once weekly  Age 12 to 17 years: 4.4 mg/kg SC loading dose followed by 2.2 mg/kg SC once weekly	Loading dose: 320 mg; Maintenance dose: 160 mg weekly
DIRA	4.4 mg/kg up to a maximum of 320 mg, delivered as 1 or 2 injections once weekly	320 mg/week

## VI. Product Availability

Single-dose vial for reconstitution: 220 mg

**VII. References**

1. Arcalyst Prescribing Information. Tarrytown, NY: Regeneron Pharmaceuticals, Inc.; March 2021. Available at [https://www.regeneron.com/sites/default/files/Arcalyst\\_FPI.pdf](https://www.regeneron.com/sites/default/files/Arcalyst_FPI.pdf). Accessed April 6, 2021.
2. Hoffman, HM, Throne ML, Amar NJ, et al. Efficacy and safety of rilonacept (interleukin-1 trap) in patients with cryopyrin-associated periodic syndromes. *Arthritis and Rheumatism*. 2008;58(8): 2443-2452.
3. Garg M, de Jesus AA, Chapelle D, et al. Rilonacept maintains long-term inflammatory remission in patients with deficiency of the IL-1 receptor antagonist. *JCI Insight*. 2017;2(16):e94838. doi: 10.1172/jc.insight.94838.
4. Adler Y, Charron P, Imazio M, et al. 2015 ESC guidelines for the diagnosis and management of pericardial diseases.
5. Klein AL, Imazio M, Cremer P, et al. Phase 3 trial of interleukin-1 trap rilonacept in recurrent pericarditis. *NEJM* 2021;384(1):31-41.

**Coding Implications**

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J2793	Injection, rilonacept, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: policies combined for Medicaid and Commercial lines of business; commercial: split from CP.CPA.234; added HIM; moved examples of positive response to therapy to Appendix C: General Information; references reviewed and updated.	02.27.18	05.18
4Q 2018 annual review: no significant changes; references reviewed and updated.	09.04.18	11.18
2Q 2019 annual review: no significant changes; references reviewed and updated.	02.26.19	05.19
2Q 2020 annual review: no significant changes; references reviewed and updated.	02.26.20	05.20
2Q 2021 annual review: RT4: added criteria for new indication of DIRA; added requirements to confirm diagnosis/severity for CAPS; added combination of bDMARDs under Section III (less rebate risk than embedding in criteria); updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	02.23.21	05.21
RT4: Criteria added for new FDA indication: treatment of RP and reduction in risk of recurrence in adults and pediatric patients 12 years and older; references reviewed and updated.	04.06.21	08.21

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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