Clinical Policy: Rilonacept (Arcalyst)

Reference Number: CP.PHAR.266
Effective Date: 11.16.16
Last Review Date: 05.22
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

Rilonacept (Arcalyst®) 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® 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 ≥ 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. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);

6. 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 ≥ 10 kg;
4. Member is in remission and has been stable for ≥ 6 months;
5. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
6. 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 ≥ 4 weeks after an acute pericarditis episode;
2. Prescribed by or in consultation with a cardiologist or rheumatologist;
3. Age ≥ 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. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
6. 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 (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member is responding positively to therapy;
3. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
4. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND

criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: 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 with biological disease-modifying antirheumatic drugs (bDMARDs) or potent immunosuppressants, including but not limited to any tumor necrosis factor (TNF) antagonists [e.g., Cimzia®, Enbrel®, Humira®, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [e.g., 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) [e.g., Xeljanz®/Xeljanz® XR, Cibinqo™, Olumiant™, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, Rituxan Hycela®], selective co-stimulation modulators [Orencia®], and integrin receptor antagonists [Entyvio®] because of the additive immunosuppression, increased risk of neutropenia, as well as increased risk of serious infections.

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
JAKi: Janus kinase inhibitors
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.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
aspirin*	**RP:** 650 – 975 mg PO TID-QID	3,900 mg/day
ibuprofen* (Advil, Motrin)	**RP:** 400 – 800 mg PO TID	2,400 mg/day
indomethacin* (Indocin)	**RP:** 50 mg PO TID	150 mg/day
colchicine*	**RP:** 0.5 mg or 0.6 mg PO BID	1.2 mg/day
prednisone*	**RP:** 0.25 – 0.5 mg/kg/day	0.5 mg/kg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) 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.accessdata.fda.gov/drugsatfda_docs/label/2021/125249s049lbl.pdf. Accessed February 17, 2022.

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. Chiabrando JG, Bonaventura A, Vecchie A, et al. Management of acute and recurrent pericarditis: JACC Sate-of-the-Art Review. *J Am Coll Cardiol* 2020; 75(1):76-92. http://doi.org/10.1016/j.jacc.2019.11..021.

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
2Q 2022 annual review: reiterated requirement against combination use with a bDMARD or JAKi from Section III to Sections I and II; references reviewed and updated.	02.16.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.13.22	

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.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.