Clinical Policy: Rilonacept (Arcalyst)

Reference Number: ERX.SPA.108
Effective Date: 10.01.16
Last Review Date: 05.22
Line of Business: Commercial, Medicaid

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 auto-inflammatory 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 weight 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.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ 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: 6 months

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 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: 6 months

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: 6 months

D. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
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: 320 mg once weekly.

Approval duration: 12 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 policy – ERX.PA.01 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 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 IL-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.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: no significant changes; 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; 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: no significant changes; reiterated requirement against combination use with a bDMARD or JAKi from Section III to Sections I and II; references reviewed and updated.	03.24.22	05.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.