Clinical Policy: Anakinra (Kineret)

Reference Number: CP.PHAR.244
Effective Date: 08.16
Last Review Date: 05.20
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Anakinra (Kineret®) is an interleukin-1 (IL-1) receptor antagonist.

FDA Approved Indication(s)

Kineret is indicated for the treatment of:

- Rheumatoid arthritis (RA): Reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active RA, in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs). Kineret can be used alone or in combination with DMARDs other than tumor necrosis factor blocking agents.
- Cryopyrin-associated periodic syndromes (CAPS): Treatment of neonatal-onset multisystem inflammatory disease (NOMID)

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 Kineret is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Rheumatoid Arthritis (must meet all)**:**

1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (*see Appendix F*);
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of at least ONE conventional DMARD (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

5. Failure of at least TWO of the following, each used for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced: Enbrel®, Kevzara®, Xeljanz®/Xeljanz XR®;
   **Prior authorization is required for Enbrel, Kevzara, and Xeljanz/Xeljanz XR*
6. Documentation of baseline clinical disease activity index (CDAI) score (*see Appendix G*);
7. Dose does not exceed 100 mg per day.

Approval duration: 6 months

B. Cryopyrin-Associated Periodic Syndromes (must meet all)**:**
1. Diagnosis of NOMID;
2. Prescribed by or in consultation with a rheumatologist;
3. Dose does not exceed 8 mg/kg per day (*see Appendix E for dose rounding guidelines*).

Approval duration: 6 months

C. 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.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 initial approval criteria;
2. Member meets one of the following (a or b):
   a. For RA member is responding positively to therapy as evidenced by a decrease in CDAI score since baseline (*see Appendix G*);
   b. For all other indications: member is responding positively to therapy;

   If request is for a dose increase, new dose does not exceed one of the following (a or b):
   c. RA: 100 mg per day;
   d. NOMID: 8 mg/kg per day (*see Appendix E for dose rounding guidelines*).

Approval duration: 12 months

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.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.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CAPS: cryopyrin-associated periodic syndromes
DMARD: disease-modifying antirheumatic drug
FDA: Food and Drug Administration
IL-1: interleukin-1
MTX: methotrexate
NOMID: neonatal-onset multisystem inflammatory disease
RA: rheumatoid arthritis

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
azathioprine (Azasan®, Imuran®)	**RA** 1 mg/kg/day PO QD or divided BID	2.5 mg/kg/day
Cuprimine® (d-penicillamine)	**RA*** Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD	1,500 mg/day
cyclosporine (Sandimmune®, Neoral®)	**RA** 2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day
hydroxychloroquine (Plaquenil®)	**RA*** Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD	600 mg/day
leflunomide (Arava®)	**RA** 100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
methotrexate (Rheumatrex®)	**RA** 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week
Ridaura® (auranofin)	**RA** 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine®)	**RA** 2 g/day PO in divided doses	3 g/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Enbrel® (etanercept)	**RA** 25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week
Kevzara® (sarilumab)	**RA** 200 mg SC once every two weeks	200 mg/2 weeks
Xeljanz® (tofacitinib)	**RA** 5 mg PO BID	10 mg/day
Xeljanz XR® (tofacitinib extended-release)	**RA** 11 mg PO QD	11 mg/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

- Contraindication(s): known hypersensitivity to *E. coli*-derived proteins, Kineret, or any components of the product
- Boxed warning(s): none reported

Appendix D: General Information

- Definition of MTX or DMARD Failure
  - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
  - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.
- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in ESR/CRP levels
  - Improvements in activities of daily living

Appendix E: Dose Rounding Guidelines for NOMID

Weight-based Dose Range	Vial Quantity Recommendation
≤ 104.99 mg	1 syringe of 100 mg/0.67 mL
105 to 209.99 mg	2 syringes of 100 mg/0.67 mL
210 to 314.99 mg	3 syringes of 100 mg/0.67 mL
325 to 419.99 mg	4 syringes of 100 mg/0.67 mL
420 to 524.99 mg	5 syringes of 100 mg/0.67 mL
525 to 629.99 mg	6 syringes of 100 mg/0.67 mL
630 to 734.99 mg	7 syringes of 100 mg/0.67 mL
735 to 839.99 mg	8 syringes of 100 mg/0.67 mL

Appendix F: The 2010 ACR Classification Criteria for RA
Add score of categories A through D; a score of ≥ 6 out of 10 is needed for classification of a patient as having definite RA.

A	**Joint involvement**	Score
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	> 10 joints (at least one small joint)	5
B	**Serology (at least one test result is needed for classification)**	
	Negative rheumatoid factor (RF) *and* negative anti-citrullinated protein antibody (ACPA)	0
	Low positive RF *or* low positive ACPA * *Low: < 3 x upper limit of normal*	2
	High positive RF *or* high positive ACPA * *High: ≥ 3 x upper limit of normal*	3
C	**Acute phase reactants (at least one test result is needed for classification)**	
	Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)	0
	Abnormal CRP or normal ESR	1
D	**Duration of symptoms**	
	< 6 weeks	0
	≥ 6 weeks	1

Appendix G: Clinical Disease Activity Index (CDAI) Score
The Clinical Disease Activity Index (CDAI) is a composite index for assessing disease activity in RA. CDAI is based on the simple summation of the count of swollen/tender joint count of 28 joints along with patient and physician global assessment on VAS (0–10 cm) Scale for estimating disease activity. The CDAI score ranges from 0 to 76.

CDAI Score	Disease state interpretation
≤ 2.8	Remission
2.8 to ≤ 10	Low disease activity
10 to ≤ 22	Moderate disease activity
> 22	High disease activity

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RA	100 mg SC QD	100 mg/day
NOMID	Initial dose: 1 – 2 mg/kg SC QD or divided BID Maintenance dose: 8 mg/kg SC QD or divided BID	8 mg/kg/day

VI. Product Availability

Single-use prefilled syringe: 100 mg/0.67 mL

VII. References

1. Kineret Prescribing Information. Stockholm, Sweden: Swedish Orphan Biovitrum AB; June 2018. Available at: http://www.kineretrx.com/pdf/Full-Prescribing-Information-English.pdf. Accessed February 26, 2020.
2. Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. Ann Rheum Dis. 2014; 73: 492-509.
3. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. Arthritis Care Res. 2012; 64(5): 625-639.
4. Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Rheumatology 2016. 68(1):1-26.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.86.Arthritis Treatments and CP.PHAR.47. CAPS. Removed criteria related to HBV, malignant disease, concomitant use with other biologics, and concurrent administration of live vaccines; added dosing requirement. RA: changed age requirement to 18 years; modified criteria to require trial of methotrexate, unless contraindicated; added sulfasalazine and hydroxychloroquine as an alternative to MTX if MTX is contraindicated; added requirement for trial and failure of PDL Enbrel and Humira, unless contraindicated. Re-auth: combined into All Indications; added criteria related to dosing per PI and reasons to discontinue. Modified approval duration to 6 months for initial and 12 months for renewal.	06.16	08.16
Converted to new template. RA: revised criteria for confirmation of RA diagnosis per 2010 ACR Criteria; added Appendix C to define MTX failure. NOMID: Added weight based dosing limit.	08.17	08.17
2Q 2018 annual review: added HIM; removed TB testing requirement from all indications; references reviewed and updated.	02.27.18	05.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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
Removed HIM line of business; updated preferred redirections based on SDC recommendation and prior clinical guidance: for RA, removed redirection to adalimumab and added redirection to 2 of 3 agents (Enbrel, Kevzara, Xeljanz/Xeljanz XR).	12.13.19	
2Q 2020 annual review: for RA, added specific diagnostic criteria for definite RA, baseline CDAI score requirement, and decrease in CDAI score as positive response to therapy; added dose rounding guidelines for NOMID; references reviewed and updated.	04.23.20	05.20

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.

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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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