Kineret (anakinra)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Kineret drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies while steering utilization to the most cost-effective medication within the therapeutic class. For this program, Humira, Enbrel, Cosentyx, Otezla, Rinvoq, Skyrizi, Stelara, Tremfya, and Xeljanz/Xeljanz XR are the preferred products and will apply to members requesting treatment for an indication that is FDA-approved for the preferred product. The criteria will require the use of two of the health plan's preferred products before the use of non-preferred products unless there are clinical circumstances that exclude the use of all the preferred products, the patient is currently receiving treatment with the non-preferred drug and experience a positive therapeutic outcome, or there is only one preferred product for an indication.

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

1. Moderately to severely active rheumatoid arthritis (RA)
2. Cryopyrin-Associated Periodic Syndromes (CAPS), including Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
3. Deficiency of Interleukin-1 Receptor Antagonist (DIRA)

Compendial Uses

1. Systemic juvenile idiopathic arthritis (sJIA)
2. Adult-onset Still's disease
3. Multicentric Castleman's disease
4. Recurrent pericarditis

5. Hyperimmunoglobulin D syndrome (HIDS) [Mevalonate Kinase Deficiency (MKD)]
6. Schnitzler's syndrome
7. CAR T-Cell Related Toxicities
8. Erdheim-Chester Disease

Required Documentation:
Submission of the following information is necessary to initiate prior authorization review:

A) Rheumatoid arthritis (RA)
1. For initial requests:
    a. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
    b. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B) Adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (sJIA):
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C) Neonatal-onset multisystem inflammatory disease (NOMID): For continuation requests: Chart notes, medical record documentation, or laboratory results supporting positive clinical response.

D) Deficiency of interleukin-1 receptor antagonist (DIRA): For initial requests: *IL1RN* mutation status.

E) Recurrent pericarditis:
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

F) Hyperimmunoglobulin D syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD): For initial requests: Chart notes, medical record documentation, or laboratory result (if applicable) indicating number of active flares within the last 6 months and Physician's Global Assessment score or C-reactive protein (CRP) level.

G) CAR T related toxicities: For initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

POLICY

Must meet BOTH the Preferred Drug Plan Design and Criteria for Initial Approval/Continuation of Therapy when both are applicable.

Preferred Drug Plan Design

A) Rheumatoid Arthritis

1. Criteria for initial approval for rheumatoid arthritis will only apply when at least ONE of the following criteria are met:
    a) Member has had an inadequate response to treatment or intolerable adverse event with at least TWO of the preferred products (Enbrel, Humira, Rinvoq, and Xeljanz/Xeljanz XR)
    b) Member has a clinical reason to avoid Enbrel and Humira (See Appendix A) AND has had an inadequate response to treatment or intolerable adverse event with the preferred products, Rinvoq AND Xeljanz or Xeljanz XR
    c) Member has a clinical reason to avoid Enbrel and Humira (See Appendix A) AND has had an inadequate response to treatment or intolerable adverse event with the preferred products, Rinvoq AND Xeljanz or Xeljanz XR
    d) Member is currently receiving treatment with the requested product through insurance (excludes obtainment as samples or via manufacturer's patient assistance programs) and experiencing a positive therapeutic outcome

Note: Submission of chart notes detailing the outcomes of treatment, intolerable adverse event(s) experienced, contraindication(s), or exclusion(s) to treatment with preferred product(s) is required (where applicable).

Criteria for Initial Approval

A) Moderately to Severely Active Rheumatoid Arthritis (RA)

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.
2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
    a. Member meets either of the following criteria:
        i. Member has been tested for either of the following biomarkers and the test was positive:
            1. Rheumatoid factor (RF)
            2. Anti-cyclic citrullinated peptide (anti-CCP)
        ii. Member has been tested for ALL of the following biomarkers:
            1. RF
            2. Anti-CCP
            3. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
    b. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week), or the member has an intolerance or contraindication to methotrexate (see Appendix B).
    c. Member has experienced an inadequate response to at least a 3-month trial of an alternative DMARD (e.g., leflunomide, hydroxychloroquine, sulfasalazine)

B) Adult-onset Still's Disease (AOSD)

Authorization of 12 months may be granted for the treatment of adult-onset Still's disease when all of the following criteria are met:

1. Member has had an inadequate response to a 3-month trial of methotrexate or corticosteroids or has intolerance or contraindication to methotrexate (see Appendix B) and low dose corticosteroids.
2. Member will receive the requested medication concurrently with methotrexate or corticosteroids or has intolerance or contraindication to methotrexate (see Appendix B) and low dose corticosteroids.

C) Active Systemic Juvenile Idiopathic Arthritis (sJIA)

1. Authorization of 12 months may be granted for treatment of active sJIA for members who have previously received a biologic indicated for active sJIA.

2. Authorization of 12 months may be granted for the treatment of active sJIA when any of the following criteria is met:
    a. Member has had an inadequate response to a 1-month trial of nonsteroidal anti-inflammatory drugs (NSAIDs)
    b. Member has had an inadequate response to a 2-week trial of corticosteroids
    c. Member has had an inadequate response to a 3-month trial of methotrexate or leflunomide

D) Neonatal-Onset Multisystem Inflammatory Disease (NOMID)

Authorization of 12 months may be granted for treatment of cryopyrin-associated periodic syndromes (CAPS), including NOMID (also known as chronic infantile neurologic cutaneous and articular syndrome [CINCA]).

E) Deficiency of interleukin-1 receptor antagonist (DIRA)

Authorization of 12 months may be granted for the treatment of genetically confirmed deficiency of interleukin-1 receptor antagonist (DIRA) due to *IL1RN* mutations.

F) Recurrent Pericarditis

Authorization of 12 months may be granted for the treatment of recurrent pericarditis for members who have failed a first-line therapy agent (i.e., colchicine).

G) Multicentric Castleman's Disease

Authorization of 12 months may be granted for the treatment of multicentric Castleman's disease when both of the following criteria are met:

1. The requested medication will be used as a single-agent.
2. The disease has progressed following treatment of relapsed/refractory or progressive disease.

H) Hyperimmunoglobulin D Syndrome (HIDS)/Mevalonate Kinase Deficiency (MKD)

Authorization of 12 months may be granted for the treatment of HIDS/MKD when all of the following criteria are met:

1. Member has had active flares within the last 6 months
2. Physician's Global Assessment greater than or equal to 2 or C-reactive protein (CRP) greater than 10 mg/L

I) Schnitzler's syndrome

Authorization of 12 months may be granted for treatment of Schnitzler's syndrome when all of the following criteria are met:

1. Member has an urticarial rash, monoclonal IgM (or IgG) gammopathy and at least two of the following signs and symptoms: fever, joint pain or inflammation, bone pain, palpable lymph nodes, enlargement of the liver or spleen, elevated numbers of white blood cells (leukocytosis), elevated red blood cell (erythrocyte) sedimentation rate or abnormalities on bone morphological study (e.g., increased bone density)
2. Other possible causes of the signs and symptoms have been ruled out, including but not limited to: hyperimmunoglobulin D syndrome, adult-onset Still disease, urticarial hypocomplementemic vasculitis, acquired C1 inhibitor deficiency and cryoglobulinemia.

J) CAR T-cell related toxicities

Authorization of 1 month may be granted for the management of G4 cytokine release syndrome that is refractory to high dose corticosteroids and anti-IL-6 therapy.

K) Erdheim-Chester Disease

Authorization of 12 months may be granted for the treatment of Erdheim-Chester disease.

Continuation of Therapy

A) Moderately to severely active rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B) Adult-onset Still's disease (AOSD) and active systemic juvenile idiopathic arthritis (sJIA)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for adult-onset Still's disease or active systemic juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability
4. Systemic symptoms (e.g., fevers, evanescent skin rashes)

C) Neonatal-onset multisystem inflammatory disease (NOMID)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for CAPS, including NOMID (also known as CINCA), and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Fever
2. Skin rash
3. Joint pain and/or inflammation
4. Central nervous system (CNS) symptoms (e.g., meningitis, headache, cerebral atrophy, uveitis, hearing loss)
5. Inflammatory markers (e.g., serum amyloid A [SAA], C-reactive protein [CRP], erythrocyte sedimentation rate [ESR])

D) Recurrent pericarditis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication t for recurrent pericarditis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following:

1. Pericarditic chest pain
2. Pericardial rubs
3. Electrocardiogram (ECG)
4. Pericardial effusion
5. C-reactive protein (CRP)

E) Multicentric Castleman's disease

Authorization of 12 months may be granted for continued treatment of multicentric Castleman's disease in members requesting reauthorization who have not experienced disease progression or an unacceptable toxicity.

F) All other indications

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for an indication outlined in the Criteria for Initial Approval and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

Other

A) For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon-release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of treatment.

B) For all indications: Member cannot use the requested medication concomitantly with any other biologic DMARD or targeted synthetic DMARD.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Kineret is considered **not medically necessary** for members who do not meet the criteria set forth above.

Quantity Limits

Trade Name	Generic Name	Quantity Limit
Kineret®	anakinra	NOMID and DIRA: Initial dosing of 1mg/kg, maintenance dosing of 3-4mg/kg and maximum dosing of 8mg/kg daily For all other indications: 28 syringes per 28 days

Appendices

Appendix A: Clinical reasons to avoid TNF-inhibitors

1. History of demyelinating disorder
2. History of congestive heart failure
3. History of hepatitis B infection
4. Autoantibody formation/lupus-like syndrome
5. Risk of lymphoma

Appendix B: Examples of Contraindications to Methotrexate

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or currently planning pregnancy
10. Renal impairment
11. Significant drug interaction

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- N/A

REFERENCES

- Kineret [package insert]. Stockholm, Sweden: Swedish Orphan Biovitrum AB (publ); December 2020.
- DRUGDEX® System (electronic version). Truven Health Analytics, Ann Arbor, MI. Available at http://www.micromedexsolutions.com [available with subscription]. Accessed November 15, 2020.
- Ringold S, Weiss PF, Beukelman T, et al. 2013 Update of the 2011 American College of Rheumatology Recommendations for the Treatment of Juvenile Idiopathic Arthritis: Recommendations for the Medical Therapy of Children With Systemic Juvenile Idiopathic Arthritis and Tuberculosis Screening Among Children Receiving Biologic Medications. *Arthritis & Rheumatism.* 2013;65:2499-2512.
- Laskari K, Tzioufas AG, Moutsopoulos HM. Efficacy and long-term follow-up of IL-1R inhibitor anakinra in adults with Still's disease: a case-series study. *Arthritis Res Ther*. 2011;13(3):R91.
- Lequerre T, Quartier P, Rosellini D, et al. Interleukin-1 receptor antagonist (anakinra) treatment in patients with systemic-onset juvenile idiopathic arthritis or adult onset Still disease: preliminary experience in France. *Ann Rheum Dis*. 2008;67:302-308.
- The NCCN Drugs & Biologics Compendium™. National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed November 15, 2020.
- Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. Ann Rheum Dis. 2020;79(6):685-699.
- 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.
- Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum.* 2008;59(6):762-784.
- Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid Arthritis Classification Criteria. An American College of Rheumatology/European League Against Rheumatism Collaborative Initiative. *Arthritis Rheum.* 2010;62:2569-2581.
- Anderson J, Caplan L, Yazdany J, et al. Rheumatoid Arthritis Disease Activity Measures: American College of Rheumatology Recommendations for Use in Clinical Practice. *Arthritis Rheum.* 2010;64:640-647.
- Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res*. 2011;63(4):465-482.
- Quartier P, Allantaz F, Cimaz R, et al. A multicentre, randomized, double-blind, placebo-controlled trial with the interleukin-1 receptor antagonist anakinra in patients with systemic-onset juvenile idiopathic arthritis (ANAJIS trial). *Ann Rheum Dis*. 2011;70:747-754.
- Efthimiou P, Paik P K, Bielory L. Diagnosis and Management of Adult Onset Still's Disease. *Ann Rheum Dis*. 2006 May;65(5):564-72. Epub 2005 Oct 11.
- National Organization for Rare Disorders. Adult Onset Still's Disease. URL: https://www.rarediseases.org/rare-disease-information/rare-diseases/byID/1210/viewFullReport. Accessed November 15, 2020.
- Adler Y, Charron P, Imazio M, et al. 2015 ESC Guidelines for the diagnosis and management of pericardial diseases: The Task Force for the Diagnosis and Management of Pericardial Diseases of the European Society of Cardiology (ESC) Endorsed by: The European Association for Cardio-Thoracic Surgery (EACTS). Eur Heart J. 2015 Nov 7;36(42):2921-64.

- Kostjukovits S, Kalliokoski L, Antila K, Korppi M. Treatment of hyperummunoglobulinemia D Syndrome with biologics in children: review of the literature and Finnish experience. Eur J Pediatr. 2015 Jun;174(6):707-14.
- National Organization for Rare Disorders. Mevalonate Kinase Deficiency. http://rarediseases.org/rare-diseases/hyper-igd-syndrome. Accessed November 15, 2020.
- American College of Rheumatology. Hyperimmunoglobulin D Syndrome. http://www.rheumatology.org/I-AM-A/Patient-Caregiver/Diseases-Conditions/Hyperimmunoglobulin-D-Syndrome-Juvenile. Accessed November 15, 2020.
- Simon A, Asli B, Braun-Falco M, et al. Schnitzler's syndrome: diagnosis, treatment, and follow-up. *Allergy*. 2013;68:562–568.
- Lipsker: The Schnitzler syndrome. *Orphanet Journal of Rare Diseases*. 2010;5:38.
- Centers for Disease Control and Prevention. Tuberculosis (TB). TB risk factors. Available at: https://www.cdc.gov/tb/topic/basics/risk.htm. Accessed: November 15, 2021.
- Lyseng-Williamson KA. Anakinra in Still's disease: A profile of its use. *Drugs Ther Perspect*. 2018;34(12):543-553.
- Yoo DH. Biologics for the treatment of adult-onset still's disease. *Expert Opin Biol Ther*. 2019 Aug 14:1-18 [Epub ahead of print].
- Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis*. 2017;76:29–42.
- Zhang W, Doherty M, Pascual E, et al. EULAR recommendations for calcium pyrophosphate deposition. Part II: Management. *Ann Rheum Dis*. 2011;70:571–575.
- Ottaviani S., Brunier L, Sibilia J, et al. Efficacy of anakinra in calcium pyrophosphate crystal-induced arthritis: A report of 16 cases and review of the literature. *Joint Bone Spine*. 2013;80:178-182.
- FitzGerald JD, Dalbeth N, Mikuls T, et al. 2020 American College of Rheumatology Guideline for the Management of Gout [published correction appears in *Arthritis Care Res (Hoboken)*. 2020 Aug;72(8):1187]. *Arthritis Care Res (Hoboken)*. 2020;72(6):744-760.
- Aksentijevich I, Masters SL, Ferguson PJ, et al. An autoinflammatory disease with deficiency of the interleukin-1-receptor antagonist. *N Engl J Med*. 2009;360(23):2426-37.
- Bonilla FA, Khan DA, Ballas ZK, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. *J Allergy Clin Immunol*. 2015;136(5):1186-205.
- Smolen JS, Aletaha D. Assessment of rheumatoid arthritis activity in clinical trials and clinical practice. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. Available with subscription. URL: www.uptodate.com. Accessed March 19, 2021.
- Fraenkel L, Bathon JM, England BR, et al. 2021 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthrit Care Res. 2021;0:1-16.

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POLICY HISTORY

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