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Section:	Prescription Drugs	**Effective Date:**	April 1, 2023
Subsection:	Analgesics and Anesthetics	**Original Policy Date:**	November 15, 2013
Subject:	Kineret	**Page:**	1 of 10

Last Review Date: March 10, 2023

Kineret

Description

Kineret (anakinra)

Background
Kineret is in a class of medications called interleukin-1 (IL-1) receptor antagonists. This means that Kineret works by blocking the activity of interleukin, a protein in the body that can induce inflammatory and immunological responses. Interleukin-1 (IL-1) is produced by the body as part of an inflammatory reaction in diseases such as Rheumatoid Arthritis (RA), Cryopyrin-Associated Periodic Syndromes (CAPS)- Neonatal-Onset Multisystem Inflammatory Disease (NOMID) and Deficiency of Interleukin-1 Receptor Antagonist (DIRA). Excess IL-1 can lead to pain, swelling, stiffness of the joints, and systemic inflammation with skin and bone involvement. Kineret can help manage the excess levels of IL-1 in the body by blocking its activity (1).

Regulatory Status
FDA-approved indications: Kineret is an interleukin-1 receptor antagonist indicated for: (1)

Rheumatoid Arthritis (RA) - Reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis, in patients 18 years of age or older who have failed 1 or more disease modifying antirheumatic drugs (DMARDs).

Cryopyrin-Associated Periodic Syndromes (CAPS) - Treatment of Neonatal-Onset Multisystem Inflammatory Disease (NOMID).

Deficiency of Interleukin-1 Receptor Antagonist (DIRA) – Treatment of Deficiency of Interleukin-1 Receptor Antagonist (DIRA).

Off-Label Uses: (2-6)
Kineret is also used off label for the following indications:

- Systemic juvenile idiopathic arthritis (sJIA)
- Adult-onset Still's disease
- Gout and pseudogout (calcium pyrophosphate deposition)
- CAR T-Cell Related Toxicities

Treatment should not be initiated in patients with an active infection and Kineret should be discontinued in patients with RA if a serious infection develops. Patients with NOMID should be assessed for the risk of a flare if Kineret therapy is discontinued against continuing treatment when an infection occurs. Concurrent use with tumor necrosis factor (TNF) blocking agents is not recommended. Hypersensitivity reactions, including anaphylactic reactions and angioedema, have been reported. Live vaccines should not be given concurrently with Kineret and neutrophil counts should be assessed prior to initiation of and during therapy (1).

Safety and efficacy of Kineret in pediatric patients for uses other than neonatal-onset multisystem inflammatory disease (NOMID) and deficiency of interleukin-1 receptor antagonist (DIRA) have not been established. Kineret is not recommended for pediatric use in juvenile rheumatoid arthritis (1).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Kineret may be considered **medically necessary** in patients with rheumatoid arthritis (RA); Cryopyrin-Associated Periodic Syndrome (CAPS) - Neonatal-Onset Multisystem Inflammatory Disease (NOMID); deficiency of Interleukin-1 Receptor Antagonist (DIRA); systemic juvenile idiopathic arthritis (sJIA); adult-onset Still's disease; gout and pseudogout; and CAR T Cell-Related Toxicities; and if the conditions indicated below are met.

Kineret may be considered **investigational** in patients that do not meet the criteria below.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Rheumatoid Arthritis (RA)
    a. 18 years of age or older
    b. Moderate to severely active
    c. Inadequate treatment response, intolerance, or contraindication to a 3-month trial of at least **ONE** conventional disease-modifying anti-rheumatic drugs (DMARDs) (see Appendix 2)
    d. Prescriber will be dosing the patient within the FDA labeled maintenance dose of 100 mg per day
    e. Patient **MUST** have tried the preferred product(s) (see Appendix 3) if adjudicated through the pharmacy benefit unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)
2. Cryopyrin-Associated Periodic Syndrome (CAPS)
    a. Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
    b. Prescriber will not exceed the FDA labeled maintenance dose of 8 mg/kg/day
3. Deficiency of Interleukin-1 Receptor Antagonist (DIRA)
    a. Prescriber will not exceed the FDA labeled maintenance dose of 8 mg/kg/day
4. Systemic juvenile idiopathic arthritis (sJIA)
5. Adult-onset Still's disease
6. Gout and pseudogout (calcium pyrophosphate deposition)
7. CAR T Cell-Related Toxicities

AND ALL of the following:

1. Result for latent TB infection is negative **OR** result was positive for latent TB and patient completed treatment (or is receiving treatment) for latent TB
2. **NO** active bacterial, invasive fungal, viral, and other opportunistic infections
3. Patient is not at risk for HBV infection **OR** patient is at risk for HBV infection and HBV infection has been ruled out or treatment for HBV infection has been initiated.
4. **NOT** to be used in combination with any other biologic DMARD or targeted synthetic DMARD (see Appendix 2)
5. **NOT** given concurrently with live vaccines

Prior – Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Rheumatoid Arthritis (RA)
   a. 18 years of age or older
   b. Prescriber will be dosing the patient within the FDA labeled maintenance dose of 100 mg per day
   c. Patient **MUST** have tried the preferred product(s) (see Appendix 3) if adjudicated through the pharmacy benefit unless the patient has a valid medical exception (e.g., inadequate treatment response, intolerance, contraindication)
2. Cryopyrin-Associated Periodic Syndrome (CAPS)
   a. Neonatal-Onset Multisystem Inflammatory Disease (NOMID)
   b. Prescriber will not exceed the FDA labeled maintenance dose of 8 mg/kg/day
3. Deficiency of Interleukin-1 Receptor Antagonist (DIRA)
   a. Prescriber will not exceed the FDA labeled maintenance dose of 8 mg/kg/day
4. Systemic juvenile idiopathic arthritis (sJIA)
5. Adult-onset Still's disease
6. Gout and pseudogout (calcium pyrophosphate deposition)
7. CAR T Cell-Related Toxicities

AND ALL of the following:

1. Condition has improved or stabilized with Kineret therapy
2. Absence of active infection (including tuberculosis and hepatitis B virus (HBV))
3. **NOT** to be used in combination with any other biologic DMARD or targeted synthetic DMARD (see Appendix 2)
4. **NOT** given concurrently with live vaccines

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Quantity

Diagnosis	Strength	Quantity
Rheumatoid Arthritis	100 mg	84 syringes per 84 days
Cryopyrin-Associated Periodic Syndrome (CAPS)	100 mg	8 mg/kg per day
Deficiency of Interleukin-1 Receptor Antagonist (DIRA)	100 mg	8 mg/kg per day
Systemic juvenile idiopathic arthritis (sJIA)	100 mg	No limit
Adult-onset Still's disease	100 mg	
Gout and pseudogout (calcium pyrophosphate deposition)	100 mg	
CAR T Cell-Related Toxicities	100 mg	

Duration 12 months

Prior – Approval *Renewal* Limits

Quantity

Diagnosis	Strength	Quantity
Rheumatoid Arthritis	100 mg	84 syringes per 84 days
Cryopyrin-Associated Periodic Syndrome (CAPS)	100 mg	8 mg/kg per day
Deficiency of Interleukin-1 Receptor Antagonist (DIRA)	100 mg	8 mg/kg per day
Systemic juvenile idiopathic arthritis (sJIA)	100 mg	No limit
Adult-onset Still's disease	100 mg	
Gout and pseudogout (calcium pyrophosphate deposition)	100 mg	
CAR T Cell-Related Toxicities	100 mg	

Duration 18 months

Rationale

Summary
Kineret is FDA-approved for the treatment of patients with Cryopyrin-Associated Periodic Syndrome (CAPS) - Neonatal-Onset Multisystem Inflammatory Disease (NOMID) and Deficiency of Interleukin-1 Receptor Antagonist (DIRA), and adult patients for the treatment of moderate to severely active rheumatoid arthritis (RA) who have had inadequate response or intolerance to

conventional therapy. Kineret is also used off-label for systemic juvenile idiopathic arthritis (sJIA), adult-onset Still's disease, gout and pseudogout, and CAR T-Cell Related Toxicities. Kineret carries warnings due to increased risk of serious infections due to immunosuppression and hypersensitivity reactions (1-6).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Kineret while maintaining optimal therapeutic outcomes.

References

1. Kineret [package insert]. Stockholm, Sweden: Swedish Orphan Biovitrum AB; December 2020.
2. 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.
3. 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.
4. 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.
5. Zhang W, Doherty M, Pascual E, et al. EULAR recommendations for calcium pyrophosphate deposition. Part II: Management. *Ann Rheum Dis*. 2011;70:571–575.
6. NCCN Drugs & Biologics Compendium® Anakinra 2023. National Comprehensive Cancer Network, Inc. Accessed on February 6, 2023.

Policy History

Date	Action
October 2013	Addition to PA
December 2013	Annual editorial review by the PMPC
September 2014	Annual editorial review and renewal limit to 18 months
December 2015	Annual editorial review and reference update, Remove moderate to severely active from renewal requirement
September 2016	Annual editorial review Addition of not given concurrently with live vaccines per SME Policy number change from 5.18.02 to 5.70.50
December 2016	Annual review and reference update
March 2017	Annual review

December 2017	Annual review
March 2017	Annual editorial review Addition of DMARD Appendix and dosing limit requirements
June 2018	Changed the inadequate response, intolerance, or contraindication to at least one conventional disease-modifying antirheumatic drugs (DMARDs) to inadequate response, intolerance, or contraindication to a 3-month trial of at least ONE conventional disease-modifying anti-rheumatic drugs (DMARDs) Updated Appendix - List of DMARDs and added Appendix - Examples of Contraindications to Methotrexate Addition of dosing requirements in renewal section
September 2018	Annual editorial review and reference update
March 2019	Annual review
December 2019	Annual review. Addition of requirement to trial preferred product
March 2020	Annual review
December 2020	Added Appendix 3 with a list of preferred medications based on diagnosis and plan. Added PA quantity limit for RA
January 2021	Addition of Indication: Deficiency of Interleukin-1 Receptor Antagonist (DIRA). Updated quantity limit table
March 2021	Annual review. Clarification added to the t/f, intolerance, C/I to preferred products requirement indicating that it only applies to claims adjudicated through the pharmacy benefit. Appendix 2 updated.
June 2021	Annual review
June 2022	Annual editorial review
September 2022	Annual review
February 2023	Per FEP, addition of off-label indications: systemic juvenile idiopathic arthritis (sJIA), adult-onset Still's disease, gout and pseudogout, and CAR T-Cell Related Toxicities
March 2023	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 10, 2023 and is effective on April 1, 2023.

Appendix 1 – Examples of Contraindications to Methotrexate

Contraindications to Methotrexate
1. Alcoholism, 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 planning pregnancy (male or female)
10. Renal impairment
11. Significant drug interaction

Appendix 2 - List of DMARDs

Conventional disease-modifying antirheumatic drugs (DMARDs)

Generic Name	Brand Name
azathioprine	Azasan, Imuran
cyclophosphamide	Cytoxan
cyclosporine	Neoral, Gengraf, Sandimmune
hydroxychloroquine	Plaquenil
leflunomide	Arava
methotrexate	Rheumatrex, Trexall
mycophenolate	Cellcept
sulfasalazine	Azulfidine, Sulfazine

Biological disease-modifying antirheumatic drugs (DMARDs)

Generic Name	Brand Name
abatacept	Orencia
adalimumab	Humira
anakinra	Kineret
brodalumab	Siliq
certolizumab	Cimzia
etanercept	Enbrel
golimumab	Simponi/Simponi Aria
guselkumab	Tremfya
infliximab	Remicade/Avsola/Inflectra/Renflexis
ixekizumab	Taltz
risankizumab-rzaa	Skyrizi
rituximab	Rituxan/Riabni/Ruxience/Truxima
sarilumab	Kevzara
secukinumab	Cosentyx
spesolimab-sbzo	Spevigo
tildrakizumab-asmn	Ilumya
tocilizumab	Actemra
ustekinumab	Stelara
vedolizumab	Entyvio

Targeted synthetic disease-modifying antirheumatic drugs (DMARDs)

Generic Name	Brand Name
apremilast	Otezla
baricitinib	Olumiant
deucravacitinib	Sotyktu

tofacitinib	Xeljanz/XR
upadactinib	Rinvoq

Appendix 3 - List of Preferred Products

Diagnosis	Standard Option/Basic Option Preferred Products	Blue Focus Preferred Products
Rheumatoid Arthritis (RA)	*must try **TWO** preferred products: Actemra (SC) (**must try Humira first**) Enbrel Humira Rinvoq Xeljanz/XR	*must try **ONE** preferred product: Enbrel Humira