



DRUG CLASS:	Disease Modifying Anti-Rheumatic Drug (DMARD)
BRAND (generic) NAME:	Kineret™ (anakinra injection)
	Kineret™ is supplied in single use 1 mL prefilled glass syringes with 27 gauge needles as a sterile, clear, colorless-to-white, preservative-free solution for daily subcutaneous administration (GCN = 014867).

FDA INDICATIONS: Anakinra is a recombinant form of human interleukin-1 receptor antagonist (IL-1Ra) indicated for the reduction in signs and symptoms of moderately to severe active rheumatoid arthritis in patients 18 years of age or older who have failed one or more disease modifying antirheumatic drugs (DMARDs). Anakinra can be used alone or in combination with DMARDs other than tumor necrosis factor (TNF) blocking agents.

OTHER USES:

- The safety and efficacy of anakinra in patients with juvenile rheumatoid arthritis (JRA) have not been established, but the drug is undergoing investigation for this indication.
- IL-1Ra is being evaluated in clinical trials as a treatment for graft-versus host disease and multiple sclerosis. It is also being tested in combination with etanercept and methotrexate.

ICD-9 CODE: Rheumatoid arthritis: 714.0

RATIONALE: The goal of RA treatment is to alleviate patient symptoms and prevent joint damage. NSAIDs (including COX-2 inhibitors) alleviate some of the symptoms of the disease but do not modify the course of the disease. Low-dose oral steroids also alleviate symptoms and may have a beneficial effect on outcomes. Disease-modifying anti-rheumatic drugs (DMARDs) are thought to potentially alter the course of the disease by reducing or preventing the occurrence of erosions and joint deformity. It typically takes 3 to 6 months before the benefits of DMARDs are seen. Traditional DMARDs include hydroxychloroquine, sulfasalazine, cyclosporine, azathioprine, D-penicillamine, auranofin, methotrexate, and gold.

BENEFIT DESIGN:

Coverage is provided **immediately** (without generating a prior authorization message) in situations where the patient is:

1. ≥ 18 years of age and,
2. A prescription for methotrexate and at least one other DMARD exists in claim history during the previous 18 months.
3. A prior authorization would **not** be generated for Kineret™ in the presence of an active claim for Enbrel®, Humira® or Remicade®.
4. Coverage would be determined in accord with the following criteria:

COVERAGE AUTHORIZATION CRITERIA:

1. Coverage provided for the treatment of moderately to severely active rheumatoid arthritis in patients ≥ 18 years of age.
2. Coverage provided in situations where the use of methotrexate and at least one other DMARD have failed to treat the patient’s rheumatoid arthritis.
3. Coverage provided in situations where the patient has had an inadequate response to methotrexate unless the use of methotrexate is contraindicated for the patient.
4. Benefit coverage **not** provided for use of Kineret™ in combination with Enbrel®, Humira® or Remicade®.

BLACK BOX WARNINGS:

None

RATIONALE:

While anakinra is indicated to relieve signs and symptoms of RA, infliximab (Remicade®) and etanercept (Enbrel®) are both indicated to relieve signs and symptoms and inhibit the progression of structural damage. There is concern that patients treated with any of the four biologics indicated for RA may be at increased risk for infection. Infliximab carries a boxed warning regarding infection. Opportunistic infections, such as tuberculosis (TB) have been reported with infliximab and etanercept, but not with anakinra. Until more information is available, co-administration with tumor necrosis factor (TNF)-blocking agents should be avoided. Studies of this combination are ongoing.

PROVIDER EDUCATION:

1. Review appropriate method for administration (subcutaneous).
2. Common adverse effects include injection site reactions, infection, headache, nausea, and diarrhea.
3. Amgen Drug Information: 800-772-6436.

DOSAGE AND ADMINISTRATION:

The recommended daily dose of anakinra for the treatment of patients with rheumatoid arthritis is 100 mg administered subcutaneously. Higher doses do not appear to yield a higher response. The dose should be administered at about the same time each day. Unused portions of the prefilled syringe should be discarded because this product does not contain a preservative. The most common adverse event in patients treated with anakinra is injection site reactions (71%), usually mild to moderate and occurring within the first 4 weeks of therapy.

RISK FACTORS/CONTRAINDICATIONS:

Kineret™ is contraindicated in patients with hypersensitivity to E.coli-derived proteins, or any product component.

Anakinra has been associated with an increased incidence of serious infections (2%) vs. placebo (<1%). Administration of anakinra should be discontinued if a patient develops a serious infection. Treatment should not be initiated in patients with active infections. The safety and efficacy of anakinra in immunosuppressed patients or in patients with chronic infections have not been evaluated. In two studies, where patients received concurrent etanercept and anakinra therapy and were treated for up to 24 weeks, a 7% rate of serious infections was observed which was higher than when either agent was used alone. Concurrent administration of anakinra and etanercept has not demonstrated increased clinical benefit.

DRUG INTERACTIONS:

- No drug interaction studies have been conducted in human subjects.
- Live vaccines should not be given concurrently with Kineret™. No data are available on the secondary transmission of infection by live vaccines in patients receiving anakinra. Since the drug interferes with normal immune response mechanisms to new antigens such as vaccines, vaccination may not be effective in patients receiving anakinra.
- There is concern that patients treated with any of the four biologics indicated for RA may be at increased risk for infection. Infliximab (Remicade®) carries a boxed warning regarding infection. Opportunistic infections, such as tuberculosis (TB) have been reported with infliximab and etanercept, but not with anakinra. Until more information is available, co-administration with tumor necrosis factor (TNF)-blocking agents should be avoided. Studies of this combination are ongoing.

REFERENCES:

1. Bresnihan B, Alvaro-Gracia JM, Cobby M et al. Treatment of rheumatoid arthritis with recombinant human interleukin-1 receptor antagonist. *Arthritis & Rheumatism*. 1998; 41: 2196-2204.
2. Product Information: Anakinra injection (Kineret™ – Amgen) 2001.