Policies Repository

AmeriHealth.

Policy Title	Anakinra (Kineret®) and Adalimumab (Humira®)
Policy Number	FS.CLIN.22

Application of Pharmacy Policy is determined by benefits and contracts. Benefits may vary based on product line, group or contract. Some medications may be subject to precertification, age, gender or quantity edits. Individual member benefits must be verified.

This Pharmacy Policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety or FDA approval may have changed. If the Medical/Pharmacy Reviewer is aware of any new information on the subject of this document, please provide it promptly to the Medical/Pharmacy Policy Department. This information may include new FDA approved indications, withdrawals or other FDA alerts. This type of information is relevant not only when considering whether this Policy should be updated, but also when applying it to current requests for coverage.

Members are advised to use participating pharmacies in order to receive the highest level of benefits.

Policy

The intent of this policy is to communicate the medical necessity criteria for anakinra (Kineret®) and adalimumab (Humira®) as provided under the member's medical benefit.

Policy Description

ANAKINRA (KINERET®)
Anakinra (Kineret®) is a synthetic, injectable interleukin-1 (IL-1) receptor antagonist that blocks the effects of human IL-1. IL-1 is a protein produced by many cells in the body, but it is found in increased amounts within joints that are inflamed from rheumatoid arthritis (RA). IL-1 attaches to receptors on the tissues within and surrounding the joints, as well as to the cells that are responsible for inflammation (eg, white blood cells). The attachment of IL-1 to its receptors activates inflammation and the release of enzymes that destroy cartilage and bone, which contributes to joint pain and swelling.

By binding to these receptors, anakinra (Kineret®) prevents the inflammatory and enzyme-releasing effects of IL-1, thereby reducing joint pain and swelling. Anakinra (Kineret®) received approval from the US Food and Drug Administration (FDA) on November 11, 2001 for the treatment of individuals with RA.

ADALIMUMAB (HUMIRA®)
Adalimumab (Humira®) is a recombinant human IgG1 monoclonal antibody that blocks tumor necrosis factor (TNF). TNF is a naturally occurring cytokine that plays a role in inflammatory and immune responses. Elevated TNF levels can cause inflammation and joint destruction in individuals with RA, ankylosing spondylitis, juvenile idiopathic arthritis, and psoriatic arthritis. Adalimumab (Humira®) binds to TNF-alpha, blocks its interaction with surface TNF receptors, and causes surface lysis (breakdown), leading to decreased inflammation and joint destruction. Adalimumab (Humira®) does not bind to or inactivate TNF-beta.

Adalimumab (Humira®) received initial FDA approval on December 31, 2002 for the treatment of individuals with RA and psoriatic arthritis. Supplemental FDA approvals have been granted for the use of adalimumab (Humira®) in the treatment of individuals who have active ankylosing spondylitis, moderately to severely active Crohn's disease, and for adults with moderate to severe chronic plaque psoriasis. It has also been approved for the treatment of moderately to

severely active polyarticular juvenile idiopathic arthritis in children 4 years of age and older.

REQUIRED DOCUMENTATION
The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to, records from the physician's office, hospital, nursing home, home health agency, other health care professionals, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation must be made available to the Company upon request.

Guidelines:

Anakinra (Kineret®) is supplied as a single-use prefilled syringe for subcutaneous injection.

Adalimumab (Humira®) is supplied as a single-use prefilled syringe for subcutaneous injection.

BENEFIT APPLICATION
Anakinra (Kineret®) and adalimumab (Humira®) are covered under the medical benefits of the Company's products when the medical necessity criteria listed in this medical policy are met.

Injectable drugs may be available under more than one benefit category; therefore, individual benefits must be verified. All applicable deductibles, coinsurance, and copayments are the member's responsibility, and the cost to members may vary based on where and how the drug is obtained.

MEDICARE
According to the Centers for Medicare & Medicaid Services (CMS), a self-administered drug is one that is usually self-administered by more than 50 percent of Medicare beneficiaries. CMS considers anakinra (Kineret®) and adalimumab (Humira®) to be self-administered drugs. These drugs are available solely under the pharmacy benefit (Part D benefit). Medicare Advantage members must have a pharmacy benefit to be eligible for coverage of anakinra (Kineret®) or adalimumab (Humira®). These drugs are not covered under the medical benefit (Part B benefit).

US FOOD AND DRUG ADMINISTRATION (FDA) STATUS
Anakinra (Kineret®) received approval from the FDA on November 11, 2001. Adalimumab (Humira®) received FDA approval on December 31, 2002; supplemental approvals have since been issued for adalimumab (Humira®).

ANAKINRA (KINERET®): WARNINGS ISSUED FROM THE MANUFACTURER AND THE FDA

The following information was taken directly from the product labeling for anakinra (Kineret®) at the time this policy was developed:

PEDIATRIC USE
The safety and efficacy of anakinra (Kineret®) in the pediatric population has not been established.

SERIOUS INFECTIONS
Anakinra (Kineret®) has been associated with an increased incidence of serious infections (2 percent) versus placebo (less than 1 percent). Administration of anakinra (Kineret®) should be discontinued if a patient develops a serious infection. Treatment with anakinra (Kineret®) should not be initiated in patients with active infections. The safety and efficacy of anakinra (Kineret®) in immunosuppressed patients or in patients with chronic infections have not been evaluated.

USE WITH TUMOR NECROSIS FACTOR (TNF)-BLOCKING AGENTS
The use of anakinra (Kineret®) in combination with TNF-blocking agents is not recommended.

ADALIMUMAB (HUMIRA®): WARNINGS ISSUED FROM THE MANUFACTURER AND THE FDA

The following information was taken directly from the product labeling for adalimumab (Humira®) at the time this policy was developed:

PEDIATRIC USE

The safety and efficacy of adalimumab (Humira®) in pediatric patients for uses other than juvenile idiopathic arthritis have not been established.

USE WITH ANAKINRA (KINERET®)

The combination of adalimumab (Humira®) and anakinra (Kineret®) is not recommended.

BLACK BOX WARNING: RISK OF SERIOUS INFECTION

Tuberculosis (frequently disseminated or extrapulmonary at clinical presentation), invasive fungal infections, and other opportunistic infections have been observed in patients receiving adalimumab (Humira®). Some of these infections have been fatal. Anti-tuberculosis treatment of patients with latent tuberculosis infection reduces the risk of reactivation in patients receiving treatment with adalimumab (Humira®). However, active tuberculosis has developed in patients receiving adalimumab (Humira®) whose screening for latent tuberculosis infection was negative.

Patients should be evaluated for tuberculosis risk factors and be tested for latent tuberculosis infection prior to initiating adalimumab (Humira®) and during therapy. Treatment of latent tuberculosis infection should be initiated prior to therapy with adalimumab (Humira®). Physicians should monitor patients receiving adalimumab (Humira®) for signs and symptoms of active tuberculosis, including patients who tested negative for latent tuberculosis infection.

Policy Guideline Inclusion

ANAKINRA (KINERET®)

Anakinra (Kineret®) is considered medically necessary and, therefore, covered for the following indications:

- **Arthritis, rheumatoid**
  For reducing signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis (RA) in individuals 18 years of age or older who have failed one or more disease-modifying antirheumatic drugs (DMARDs). Anakinra (Kineret®) can be used alone or in combination with DMARDs, with the exception of other tumor necrosis factor (TNF)-blocking agents.

- **Arthritis associated with other conditions**
  For reducing signs and symptoms of arthritis associated with any of the following conditions:
  - Inflammatory bowel disease
  - Crohn's disease
  - Reiter's syndrome
  - Other post-infectious syndromes

ADALIMUMAB (HUMIRA®)

Adalimumab (Humira®) is considered medically necessary and, therefore, covered for the following indications:

- **Arthritis, rheumatoid**
  For reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in individuals 18 years of age or older who have moderately to severely active RA

- **Arthritis, psoriatic**
  For reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in individuals with active psoriatic arthritis

- **Arthritis associated with other conditions**
  For reducing signs and symptoms of arthritis associated with any of the following conditions:
  - Inflammatory bowel disease
  - Crohn's disease
  - Reiter's syndrome
  - Other post-infectious syndromes

- **Ankylosing spondylitis**
  For reducing signs and symptoms in individuals with active ankylosing spondylitis

- **Crohn's disease**
  For reducing signs and symptoms of disease, and inducing and maintaining clinical remission in adults with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy, or who no longer respond to or are intolerant to infliximab (Remicade®)

- **Juvenile idiopathic arthritis**
  For reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in children 4 years of age and older

- **Plaque psoriasis**
  In the treatment of adults with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate.

Policy Guideline Exclusion

EXPERIMENTAL / INVESTIGATIONAL
All other uses for anakinra (Kineret®) or adalimumab (Humira®) are considered experimental/investigational and, therefore, not covered because the safety and/or efficacy of these drugs for those uses cannot be established by review of the available published medical literature.

The use of adalimumab (Humira®) with other TNF-blocking agents (eg, infliximab [Remicade®], etanercept [Enbrel®]) or interleukin-1 (IL-1) inhibitors (eg, anakinra [Kineret®]) is considered experimental/investigational and, therefore, not covered because the safety and/or efficacy of this regimen cannot be established by review of the available published medical literature.

Policy List of Applicable Drugs

Brand Name	Generic Name
Kineret	anakinra
Humira	adalimumab

Dosing and Administration

Refer to the specific manufacturer's prescribing information for administration and dosage details, contraindications, and Black Box warnings.

Policy References

American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. [American College of Rheumatology Web site]. Available at: http://www.rheumatology.org/publications/guidelines/raguidelines02.asp?aud=mem. Accessed February 28, 2008.

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Policy Link to Related Policies

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