



# CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Effective Date ..... 7/15/2011  
Next Review Date ..... 7/15/2012  
Coverage Policy Number ..... 4063

Subject **Anakinra (Kineret®)**

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## Hyperlink to Related Coverage Policies

Actemra®  
 Cimzia®  
 Enbrel®  
 Humira®  
 Orencia®  
 Remicade®  
 Rituxan®  
 Simponi™

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

**CIGNA covers anakinra (Kineret®) as medically necessary for the treatment of active rheumatoid arthritis (RA) in adults when EITHER of the following indications is met:**

- history of a beneficial clinical response to anakinra
- inadequate response intolerance, or contraindication to at least **ONE** disease-modifying anti-rheumatic drugs (DMARDs) (i.e., Methotrexate (MTX) Azathioprine, gold, Hydroxychloroquine, Leflunomide, Penicillamine, Sulfasalazine) **AND** to **TWO self-administered preferred** tumor necrosis factor (TNF) antagonists [adalimumab (Humira®) and etanercept (Enbrel®)]

**CIGNA does not cover anakinra (Kineret®) for treatment of any of the following conditions because it is considered experimental, investigational or unproven (this list may not be all-inclusive):**

- reactive arthritis
- inflammatory bowel disease
- ankylosing spondylitis

**The dosage, frequency, site of administration, and duration of therapy are reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to anakinra (Kineret®) therapy.**

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### **FDA Approved Indications**

Kineret is indicated for the 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). Kineret can be used alone or in combination with DMARDs other than Tumor Necrosis Factor (TNF) blocking agents.

### **FDA Recommended Dosing**

The recommended dose of Kineret for the treatment of patients with rheumatoid arthritis is 100 mg/day administered daily by subcutaneous injection. Higher doses did not result in a higher response. The dose should be administered at approximately the same time every day.

### **Drug Availability**

Kineret is supplied in single-use preservative free, prefilled glass syringes with 27 gauge needles. Each prefilled glass syringe contains 0.67 mL (100 mg) of anakinra. Kineret is dispensed in a 4 x 7 syringe dispensing pack containing 28 syringes.

### **General Background**

#### **Pharmacology**

Kineret blocks the biologic activity of IL-1 by competitively inhibiting IL-1 binding to the interleukin-1 type I receptor (IL-1RI), which is expressed in a wide variety of tissues and organs.<sup>1</sup> IL-1 production is induced in response to inflammatory stimuli and mediates various physiologic responses including inflammatory and immunological responses. IL-1 has a broad range of activities including cartilage degradation by its induction of the rapid loss of proteoglycans, as well as stimulation of bone resorption.<sup>2</sup> The levels of the naturally occurring IL-1Ra in synovium and synovial fluid from rheumatoid arthritis (RA) patients are not sufficient to compete with the elevated amount of locally produced IL-1.

#### **Guidelines**

##### **American College of Rheumatology (ACR)**

The American College of Rheumatology (ACR) 2010 recommendations include the use of nonbiologic and biologic therapies in patients with RA when starting or resuming these therapies. The 2010 ACR recommendations address five key areas including: the indications for use, monitoring for side-effects, screening for tuberculosis which is a risk factor associated with biologic DMARDs, and off-label uses. The duration of RA disease duration, disease severity, and prognostic features were also considered when developing these recommendations. According to ACR guideline, it is important that RA patients be seen regularly to assess disease activity, evaluate disease severity, and determine whether alternative therapies are warranted. Because there was no evidence to support a specific recommendation on the frequency of provider visits, a specific and potentially arbitrary time frame is not recommended at this point. However, based on these recommendations, commonly used but not exclusive tools to assess the RA disease activity include: Disease Activity Score (DAS) in 28 joints, Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Rheumatoid Arthritis Disease Activity Index, Patient Activity Scale (PAS), and Routine Assessment Patient Index Data. In addition it is recommended to use the combinations of commonly used but not exclusive prognostic factors to evaluate the patients with RA, including: Health Assessment Questionnaire (HAQ) score, Evidence of radiographic erosions, Elevated erythrocyte sedimentation rate, Elevated C-reactive protein level, and elevated levels of rheumatoid factor (RF) and/or anti-cyclic citrullinated peptide (anti-CCP) antibodies. Due to the absence of a single "gold standard" measure, multiple measures or pooled indices are used to determine a diagnosis, estimate prognosis, and to assess and monitor disease activity and response to treatment. Other commonly used measures in the clinical settings include: Visual Analogue scale (VAS), Likert scales of global response to pain by the patient/doctor, and Global Arthritis Score (GAS).

Many autoimmune rheumatic diseases have severe multisystem manifestations, including internal organ involvement and premature death. Unfortunately, for many of these conditions, standard (FDA approved)

therapies do not exist, or are only effective in a subset of patients. The rarity of some of these conditions presents a barrier to performing large scale studies required for regulatory approval. However, valuable information is obtained in the published clinical reports of biologic DMARD therapies for many less common but disabling autoimmune conditions. When successful treatment options have been clearly documented in peer-reviewed journals, patients should receive the opportunity to benefit from these effective therapies.

While the American College of Rheumatology (ACR) offers a model for recommended off-label coverage criteria for use of TNF's. Other uses where TNF products have shown efficacy of use have not been shown with this product. Therefore, any other use for this product that is not listed in the criteria coverage stem is considered experimental, investigational, and unproven.

### **Adverse Reactions**

Anakinra should also not be used in combination with anti-TNF agents due to an increased risk of neutropenia and serious infection. These agents should be used with caution when used with other agents that could suppress the immune system or in patients who are immunocompromised. Live vaccines should not be administered to patients taking any of the BRMs.

Anakinra, like other BRMs, has warnings due to rare occurrences of serious infections and sepsis associated with the use of anti-TNF agents. Therapy should not be initiated in patients with active infections, and therapy should be discontinued if a serious infection or sepsis develops. Small reductions in the white blood cell count (WBC), platelets, and absolute neutrophil count (ANC) and small increases in the mean eosinophil differential percentage were observed in the placebo-controlled trials with anakinra.

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## **Coding/Billing Information**

**Note:** This section is not in use.

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## **References**

1. American College of Rheumatology (ACR). Model Biologics Policy, 2010.
2. Amgen I. Anakinra (Kineret) injection package insert. Thousand Oaks, CA: Amgen. Dec 2009.
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## Policy History

<b>Pre-Merger Organizations</b>	<b>Last Review Date</b>	<b>Policy Number</b>	<b>Title</b>
CIGNA HealthCare Great-West Healthcare	7/15/2008	4063	Anakinra (Kineret®)

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