Cigna Pharmacy Coverage Policy

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Coverage Policy Number: 4063

Subject: Anakinra (Kineret®)

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Tumor Necrosis Factor Antagonist Therapy

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna companies including plans formerly administered by Great-West Healthcare, which is now a part of Cigna. Coverage Policies are intended to provide guidance in interpreting certain standard Cigna benefit plans. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, 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 ©2012 Cigna

Coverage Policy

Cigna covers anakinra (Kineret®) as medically necessary for the treatment of active rheumatoid arthritis (RA) in an adult 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

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to anakinra (Kineret®).
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. 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. 2 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 ACR updated their 2008 recommendations for the use of DMARDs and biologic agents in the treatment of RA in April 2012. The updated recommendations follow the same methodology used to develop the 2008 recommendations. While the recommendations are extensive and include new areas and new agents not covered in 2008, they are not comprehensive and should be used as a guide for clinicians treating RA patients.

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. 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 anticyclic 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).

The ACR plans to periodically update RA treatment recommendations depending upon the availability of new therapies, new evidence on the benefits and harms of existing treatments, and changes in policies to reflect the rapidly evolving care of RA patients. The 2012 revision updates the 2008 recommendations in the following areas:

- indications for DMARDs and biologic agents
- switching between DMARD and biologic therapies
- use of biologic agents in high-risk patients (those with hepatitis, congestive heart failure [CHF], and malignancy)
- screening for TB in patients starting or currently receiving biologic agents
- vaccination in patients starting or currently receiving DMARDs or biologic agents

Though recommendations vary with each patient, the 2012 guidelines generally recommend physicians start treatment with a DMARD, proceed to therapy combining two or more DMARDs and then to a biologic when and if each option fails to control the disease. When switching from DMARDs to biologics, for example, physicians should use either an anti-TNF biologic or a non-TNF biologic if a patient has moderate or high disease activity after three months of methotrexate treatment or DMARD combination therapy.

For use in high-risk patients, the guideline recommendations go against the use of biologics in RA patients with untreated chronic hepatitis B or with treated chronic hepatitis B with Child-Pugh class B and higher because of the potential for strong side-effects. Etanercept is the only biologic recommended for use in RA patients with Hepatitis C.

RA patients with cancer may be treated with a biologic if their treatment for a solid malignancy was over 5 years ago or treated non-melanoma skin cancer was over 5 years ago. Rituximab is recommended for patients treated for a solid malignancy within the last 5 years or treated non-melanoma skin cancer within the last 5 years, treated skin melanoma, or treated lymphoproliferative malignancy.

Recommendations for patients with heart failure include a biologic if their case is not too severe. However, a biologic is not recommended for patients with a NYHA class III/IV rating and an ejection fraction of less than or equal to 50%.

Due to increasing awareness of the risk of preventable infections in RA patients, the recommendations place a priority on screening and vaccination. RA is an autoimmune disease in which the immune system attacks the body's own tissues. Treatments suppress the immune system and make those treated vulnerable to infections. For that reason, the 2012 guidelines recommend that all patients taking biologics for RA be screened for latent tuberculosis infection (LTBI) – statistics show that 5 to 10 percent of these patients will go on to develop active TB later.

The 2012 guidelines recommend that all killed (pneumococcal, influenza intramuscular, and hepatitis B), recombinant (human papillomavirus [HPV] vaccine for cervical cancer) and live attenuated (herpes zoster) vaccinations should be undertaken before starting a DMARD or a biologic agent. If not previously done, vaccination with indicated pneumococcal (killed), influenza intramuscular (killed), hepatitis B (killed), and HPV vaccine (recombinant) should be undertaken in RA patients already taking a DMARD or a biologic agent. Vaccination with herpes zoster vaccine in RA patients already taking a DMARD is recommended but is not recommended in patients taking a biologic agent. All vaccines should be given based on age and risk, and physicians should refer to vaccine instructions and CDC recommendations for details about dosing and timing issues related to vaccinations.

The 2012 guidelines literature search included eight DMARDs and nine biologic agents most commonly used for the treatment of RA. DMARDs included azathioprine, cyclosporine, hydroxychloroquine, leflunomide, methotrexate, minocycline, organic gold compounds, and sulfasalazine. Similar to 2008, azathioprine, cyclosporine, and gold were not included in the recommendations based on their infrequent use and lack of new data. The biologic agents included abatacept, adalimumab, anakinra, certolizumab pegol, etanercept, golimumab, infliximab, rituximab, and tocilizumab. Anakinra was not included in the recommendations due to infrequent use and lack of new data.

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. The most common adverse reactions are injection site reaction, worsening of rheumatoid arthritis, upper respiratory tract infection, headache, nausea, diarrhea, sinusitis, arthralgia, flu like-symptoms, and abdominal pain.

Coding/Billing Information

Note: Kineret is typically covered under pharmacy benefit plans. Certain prescription drugs require an authorization for coverage to ensure that appropriate treatment regimens are followed. Medical drug coding and diagnosis codes, however, are generally not required for pharmacy claims submissions, therefore, this section is not in use.

References

## Policy History

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