**Kineret® Step Therapy Criteria**

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<tr>
<th>Brand</th>
<th>generic</th>
<th>Dosage Form</th>
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<tr>
<td>Kineret®</td>
<td>anakinra</td>
<td>injection</td>
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**FDA Approved Indications**

Kineret® (anakinra) 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 one or more disease modifying antirheumatic drugs (DMARDs). Kineret may be used alone or in combination with DMARDs other than Tumor Necrosis Factor (TNF) blocking agents.

**Rationale for selecting Kineret for Step Therapy**

The intent of the Kineret Step Therapy Criteria is to ensure that patients prescribed therapy are properly selected according to FDA-approved product labeling and/or clinical guidelines and/or clinical trials. Kineret is indicated for moderately to severely active rheumatoid arthritis patients who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs). Kineret may be used alone or in combination with methotrexate or other DMARD’s except Tumor Necrosis Factor (TNF) blocking agents.

The American College of Rheumatology (ACR) guidelines for the management of rheumatoid arthritis recommend initiation of DMARD therapy within three months of diagnosis for the majority of patients. DMARDs have the potential to reduce or prevent joint damage and preserve joint integrity and function. Other traditional pharmacologic treatments such as nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoid joint injection, and/or low-dose prednisone have analgesic and anti-inflammatory properties but do not alter the progression of the disease or prevent joint destruction. These agents should be used for symptom control.

ACR guidelines suggest that the patient and physician select the initial DMARD based on its relative efficacy, convenience of administration, requirements of monitoring, costs, time until expected benefit, and frequency and potential seriousness of adverse reactions. The physician should also consider patient compliance, comorbid diseases, severity and prognosis of the patient’s disease and the physician’s own expertise in administering and monitoring the agent. Many rheumatologists select methotrexate as the initial DMARD because of the proven efficacy of the agent and tolerability. For patients with very active disease or with indicators for a poorer prognosis (e.g., earlier age at disease onset, high titer of rheumatoid factor, elevated erythrocyte sedimentation rate, or swelling of greater than 20 joints), initial treatment with methotrexate or combination therapy is preferred. Inadequate response to maximum therapy after three months of treatment indicates the need for change or addition of another DMARD. Methotrexate as monotherapy or as a component of combination therapy may be instituted in methotrexate-naive patients. If methotrexate is contraindicated or if methotrexate treatment has failed to achieve satisfactory disease control because of lack of efficacy or because of patient intolerance, treatment with biologic agents such as Kineret or other DMARDs, alone or in combination is indicated.
The Kineret Step Therapy Criteria has been designed to allow for the automatic payment of Kineret without prior authorization for those patients who have a claim for methotrexate or Kineret in their drug history within the previous 90 days of the Kineret claim or who are currently being treated with methotrexate.

Recommendations for the use of Tumor Necrosis Factor (TNF) blocking agents for the treatment of rheumatoid arthritis and other rheumatic diseases were outlined in a consensus statement developed at a worldwide conference of rheumatologists and bioscientists for publication in Annals of Rheumatic Diseases. The consensus statement recommends the use of TNF blockers for the treatment of active RA after an adequate trial of another effective DMARD, usually methotrexate. TNF blocking agents may be added to pre-existing treatment, or replace previous DMARDs, when appropriate. The consensus statement did not recommend TNF agents as the first DMARD for treatment of RA because of considerations for long-term safety and cost unless other DMARDs are contraindicated for the patient. A systematic analysis evaluating Enbrel, Remicade, and Humira, showed similar efficacy when added to methotrexate for the treatment of active rheumatoid arthritis. There have been no head-to-head trials or systematic reviews comparing the efficacy of Kineret to the TNF blocking agents.

**Initial Automatic Step Therapy Edit Functionality**

The step therapy process requires that another drug or drugs must be tried for a specific quantity in a specific time period prior to the claim drug. If the patient has met the requirements defined below, the requested step therapy medication will be paid automatically under the patient’s current prescription drug benefit. If the step therapy edit is not met, a Point of Sale message will be returned to the pharmacy stating the step is not met and prior authorization is required. The Prior Authorization (PA) Criteria for Approval would then be applied to requests submitted by the patient’s practitioner for evaluation.

Kineret® edit
In order for a claim for Kineret to pay automatically, the patient must have medication history of a previous claim for injectable methotrexate (GPI 21300050******) or oral methotrexate (GPI 66250050******) or Kineret (GPI 66260010******) within 90 days prior to the Kineret claim. The claims system is designed to identify and count any methotrexate or Kineret claim with a days supply that ends in the 90-day look-back parameter. The 90-day parameter is intended to identify recent or concurrent therapy and prevent disruption of previously established Kineret therapy. The Kineret claim will be rejected for payment if there is a claim in the patient’s medication history for Enbrel, Humira, or Remicade whose days supply overlaps a 30-day look-back period.

**Clinical Rationale for Step Therapy Functions**

**Step Therapy Electronic Edit**

The intent of the initial step therapy edit is to electronically identify patients who have a medication history of methotrexate or Kineret filled within 90 days prior to the Kineret claim. The 90-day parameter for methotrexate was selected because ACR guidelines recommend the periodic reassessment of patients for evidence of disease activity or progression and for toxic effects of the treatment regimen. Ongoing disease activity or progressive joint damage after 90 days of maximum therapy indicate a need for changes in the DMARD regimen.

**Prior Authorization (PA) Criteria for Approval**

**Initial Approval Criteria**

The intent of the Prior Authorization Criteria for Kineret is to ensure that patients prescribed therapy meet the selection criteria noted in labeling and/or clinical trials and/or guidelines. ACR guidelines for the management of RA indicate Kineret as a second-line agent for therapy after inadequate response to methotrexate or other DMARDs. The Prior Authorization Criteria will require the prior use of methotrexate. Initial approval will be for 90 days since ACR guidelines
recommend reassessment and change of therapy if there is inadequate response after 3 months. Renewal of therapy will be for 12 months.

Product labeling for Kineret does not support the concomitant use of Kineret with Enbrel. In a study evaluating concurrent use, the rate of serious infection was higher in the combination arm compared to Enbrel alone (7% versus 0%, respectively). Combination therapy did not demonstrate higher ACR response rates compared to Enbrel alone. There is no literature evaluating combination therapy with Enbrel and Humira or Remicade. Active claims for Humira, Enbrel, and Remicade will be discontinued prior to the approval for Kineret.

Prior Authorization Criteria for Approval

**Kineret**

**Initial and Renewal Evaluation**

1. Has the patient been prescribed Kineret in the past 90 days?
   - If yes, approve for 12 months. If no, continue to 2.

2. Does the patient have a diagnosis of rheumatoid arthritis?
   - If yes, continue to 3. If no, approve for 3 months.

3. Is Kineret being used with methotrexate to treat the patient?
   - If yes, continue to 5. If no, continue to 4.

4. Does the patient have a treatment failure, allergy, intolerance or contraindication to methotrexate therapy (e.g., pregnancy, breast feeding, alcoholism, chronic liver disease, chronic hepatitis B or C infection, or persistently elevated liver function tests, leukopenia, thrombocytopenia, diarrhea or anemia) or does the physician or patient refuse treatment with methotrexate due to possible adverse effects?
   - If yes, continue to 5. If no, deny.

5. Has the patient been previously treated with Humira, Enbrel or Remicade and therapy is now being switched to Kineret?
   - If yes, continue to 6. If no, approve for 3 months.

6. Will Humira, Enbrel or Remicade be discontinued before starting Kineret?
   - If yes, approve for 3 months. If no, deny.

**Conclusion**

Step therapy electronic edits are designed to identify patients electronically by their medication history. The Kineret Step Therapy edit allows for automatic payment of claims when the patient’s medication history indicates prior use of methotrexate or Kineret, bypassing the manual PA process. The PA process provides a member-specific review process where practitioner provided patient-specific parameters are taken into consideration and are reviewed by a physician.

**References**

4. Hochberg MC, Tracy JK, Hawkins-Holt M, Flores RH. Comparison of the efficacy of the tumour necrosis factor alpha blocking agents adalimumab, etanercept, and infliximab


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<tr>
<th>Document History</th>
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<tr>
<td>Original Prime Standard Approved by UMC 08/2004</td>
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