Humira®
Step Therapy Criteria

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<tr>
<th>Brand</th>
<th>generic</th>
<th>Dosage Form</th>
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<tbody>
<tr>
<td>Humira®</td>
<td>adalimumab</td>
<td>injection</td>
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FDA Approved Indications
Humira® (adalimumab) is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs). Humira can be used alone or in combination with methotrexate or other DMARDs. Humira is also indicated for reducing the signs and symptoms of active arthritis in patients with psoriatic arthritis. Humira can be used alone or in combination with DMARDs.

Rationale for selecting Humira for Step Therapy
The intent of the Humira 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. Humira is indicated for moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs). Humira may be used alone or in combination with methotrexate or other DMARDs.

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.
patients.² 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 Humira or other DMARDs, alone or in combination is indicated.²

The Humira Step Therapy Criteria has been designed to allow for the automatic payment of Humira without prior authorization for those patients who have a claim for methotrexate or Humira in their drug history within the previous 90 days of the Humira 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.*³ 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.³ 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.³ A systematic analysis evaluating Enbrel, Remicade, and Humira, showed similar efficacy when added to methotrexate for the treatment of active rheumatoid arthritis.³ 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 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.

**Humira® edit**

In order for a claim for Humira to pay automatically, the patient must have medication history of a previous claim for injectable methotrexate (GPI 21300050******) or oral methotrexate (GPI 66250050******) or previous Humira (GPI 66270015******) therapy within 90 days prior to the Humira claim. A look-back parameter of 90 days is intended to identify recent or current methotrexate or Humira therapy and to prevent disruption of established Humira therapy. The claims system is designed to identify and count any methotrexate or Humira claim with a days supply that ends within the 90-day look-back parameter. The claim will be rejected for payment if there is a claim in the patient’s medication history for Enbrel, Kineret, 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 Humira filled within 90 days prior to the Humira claim.

**Rationale for the Humira edit**

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.² ACR guidelines for the management of RA indicate biologic agents as second-line therapy after inadequate response to methotrexate or other DMARDs.² Ongoing disease activity or progressive joint damage after 90 days of maximum therapy indicate a need for changes in the DMARD regimen.²
Prior Authorization (PA) Criteria for Approval

Initial Approval Criteria

The intent of the Prior Authorization Criteria for Humira 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 Humira as a second-line agent after an inadequate response to methotrexate or other DMARDs. 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.

For patients who have been on Enbrel, Kineret or Remicade and are being switched to Humira, a sufficient wash-out period (determined by physician) will be required before initiating therapy. There are no studies supporting concomitant therapy with Humira and Enbrel or Kineret or Remicade. Active claims for Enbrel, Kineret, or Remicade will be discontinued before prior authorization for Humira will be granted.

Prior Authorization Criteria for Approval

Humira

Initial and Renewal Evaluation

1. Has the patient been prescribed Humira 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 or psoriatic arthritis?
   If yes, continue to question 3. If no, approve for 3 months

3. Is the patient currently treated with methotrexate combined with Humira?
   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 treated previously with Enbrel, Kineret or Remicade and therapy is now being switched to Humira?
   If yes, continue to 6. If no, approve for 3 months.

6. Will the Enbrel, Kineret or Remicade be discontinued before starting Humira?
   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 Humira Step Therapy edit allows for automatic payment of claims when the patient’s medication history indicates prior use of methotrexate or Humira, 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

**Document History**

- Original Prime Standard Approved by UMC 08/2004
- Client specific modifications 07/2005
- Annual Review with changes Approved by External UMC 11/2005
- Annual Review with changes, Client Specific criteria approved by HCSC Corporate Clinical Committee 12/2005