Enbrel®
Step Therapy Criteria

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<th>Brand</th>
<th>generic</th>
<th>Dosage Form</th>
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<td>Enbrel®</td>
<td>etanercept</td>
<td>injection</td>
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**FDA Approved Indications**

Enbrel® (etanercept) is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis. Enbrel may be used in combination with methotrexate in patients who do not respond adequately to methotrexate alone.

Enbrel is indicated for reducing signs and symptoms of moderately to severely active polyarticular-course juvenile rheumatoid arthritis in patients who have had an inadequate response to one or more disease-modifying antirheumatic drugs (DMARDs).

Enbrel is indicated for reducing signs and symptoms and inhibiting the progression of structural damage of active arthritis in patients with psoriatic arthritis. Enbrel may be used in combination with methotrexate in patients who do not respond adequately to methotrexate alone.

Enbrel is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

Enbrel is indicated for the treatment of adult patients (18 years or older) with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

Unlabeled uses: Juvenile spondyloarthropathies.

**Rationale for selecting Enbrel for Step Therapy**

The intent of the Enbrel 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. Enbrel is indicated for the treatment of several classifications of arthritis including moderately to severely active rheumatoid arthritis, moderately to severely active polyarticular-course juvenile arthritis, psoriatic arthritis, ankylosing spondylitis, and also for chronic moderate to severe plaque psoriasis. Enbrel is generally not a first line treatment for rheumatoid arthritis or for plaque psoriasis. Product labeling recommends that Enbrel be used in combination with methotrexate for the treatment of rheumatoid arthritis or psoriatic arthritis in patients who do not adequately respond to methotrexate alone. Enbrel may be used in patients with juvenile rheumatoid arthritis who have not adequately responded to one or more disease modifying anti-rheumatic drugs (DMARDs). The majority of patients with plaque psoriasis are successfully treated with topical agents, predominantly corticosteroids, which are considered first-line therapy. Other effective topical agents include coal tars, calcipotriene ointment, tazarotene, and intralosional corticosteroid injections. Product labeling recommends use of Enbrel for plaque psoriasis for those patients who are candidates for systemic or phototherapy.
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 Enbrel or other DMARDs, alone or in combination is indicated.

The Enbrel Step Therapy Criteria has been designed to allow for the automatic payment of Enbrel without prior authorization for those patients who have a claim for methotrexate or Enbrel in their drug history within the previous 90 days of the Enbrel claim or who are currently being treated with methotrexate. A claim for Enbrel will also pay automatically if the patient has a previous medication history indicating use of a topical or systemic antipsoriatic agent 180 days prior to the Enbrel claim.

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. Concomitant therapy with Enbrel and Kineret is not recommended. There are no clinical studies supporting the concomitant use of Enbrel and Humira.

The majority of patients experiencing active psoriasis can be successfully managed with topical therapy. Corticosteroids are the most commonly prescribed therapy for psoriasis and in treatment algorithms for the disease, corticosteroids are considered initial therapy. Alternatives to topical corticosteroids, which may cause skin atrophy, include the following; coal tars; calcipotriene ointment, a synthetic vitamin D₃ analogue; tazarotene, a topical retinoid; anthralin; and intralesional corticosteroid injections. When patients have psoriasis that is refractory to topical therapy or affected areas are too widespread for topical treatment, phototherapy or systemic therapy are generally prescribed. Alternatives include combination therapy with oral or topical psoralens and UVA radiation (PUVA) and systemic agents such as methotrexate,
cyclosporine, and the retinoid, acitretin. Enbrel is indicated for the treatment of adult patients with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.¹

**Initial Automatic Step Therapy Edit Functionality**

The step therapy process requires that for a claim to pay automatically, 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 any of the requirements outlined below, the requested step therapy medication will be paid automatically under the patient’s current prescription drug benefit. If the patient does not meet the step therapy criteria, then the system will reject with the message indicating that 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.

**Enbrel® edits**

A. In order for a claim for Enbrel 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 Enbrel (GPI 66290030******) within 90 days prior to the Enbrel claim. The claims system is designed to identify and count any methotrexate or Enbrel claim with a days supply that ends within the 90-day look-back parameter. The 90-day parameter is intended to capture recent or concurrent therapy and to prevent disruption of previously established therapy with Enbrel. The claim will not pay automatically if, included in the medication history, there is a claim for Humira, Kineret, or Remicade whose days supply overlaps a 30-day look-back period.

B. A claim for Enbrel will also pay automatically if the medication history includes a claim for a topical or systemic antipsoriatic agent within the previous 180 days (six months). Topical treatments that will allow automatic payment for Enbrel includes coal tar products (GPI 9052**********), anthralin, (GPI 902500*********), topical corticosteroids, (GPI 9055*********), calcipotriene, (GPI 902500*********), and tazarotene, (GPI 902500*********). Systemic treatments include methotrexate (GPI 21300050****** or 66250050******), cyclosporine (GPI 9940202030****), acitretin (GPI 90250510******), or methoxsalen (GPI 90250560******).

**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 Enbrel filled within 90 days prior to the Enbrel claim or a medication history of a topical or systemic antipsoriatic agent filled within 180 days of the Enbrel claim.

**Rationale for edit A.**

The 90-day parameter for methotrexate was selected because ACR guidelines recommend the periodic reassessment of patients within 90 days for evidence of disease activity or progression and for toxic effects of the treatment regimen.² Ongoing disease activity or progressive joint damage after 90 days of maximum therapy indicates a need for changes in the DMARD therapy.²

**Rationale for edit B**

Plaque psoriasis is a disease with symptoms that wax and wane and may require only intermittent therapy. Therefore, the edit will search medication history 180 days prior to the Enbrel claim for topical or systemic antipsoriatic agents.

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

**Initial Approval Criteria**

The intent of the Prior Authorization Criteria for Enbrel is to ensure that patients prescribed therapy meet the selection criteria noted in labeling and/or clinical trials and/or guidelines. Use of Enbrel will be limited to the labeled diagnosis of Rheumatoid Arthritis, juvenile Rheumatoid Arthritis, psoriatic arthritis, ankylosing spondylitis (AS), and plaque psoriasis.¹ ACR guidelines for
the management of RA indicate Enbrel as a second-line agent for therapy after inadequate response to methotrexate or other DMARDs. Treatment algorithms for plaque psoriasis therapy recommend topical agents before systemic treatment or phototherapy. The prior authorization criteria will approve the administration of Enbrel if the patient has had an inadequate response to methotrexate or a topical or systemic antipsoriatic agent. Recommendations for the treatment of AS do not include the use of DMARDs other than sulfasalazine. Enbrel will be approved for this diagnosis without previous trial of any other agent. Initial approval will be for 90 days since ACR guidelines recommend reassessment and change of therapy if there is inadequate response after 3 months. Clinical trials evaluating Enbrel for the treatment of plaque psoriasis assessed initial response at 3 months. Renewal of therapy will be for 12 months.

Product labeling for Enbrel does not support the concomitant use of Enbrel with Kineret. 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. Active claims for Humira, Kineret, and Remicade will be discontinued prior to the approval for Enbrel.

For patients who have been on another TNF antagonist and are being switched to Enbrel, a sufficient wash-out period (determined by physician) will be required before initiating therapy. Concomitant TNF antagonist therapy will be denied.

**Prior Authorization Criteria for Approval**

**Enbrel**

**Initial and Renewal Evaluation**

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

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

3. Is Enbrel being used concurrently with methotrexate to treat the patient?
   - If yes, approve for 3 months. 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 6. If no, continue to 5.

5. Does the patient have treatment failure, intolerance, allergy or contraindication to topical or systemic antipsoriatic agents (e.g., topical corticosteroids, topical coal tar products, tazarotene, cyclosporine, methoxsalen, anthralin, calcipotriene, methotrexate or acitretin).
   - If yes, continue to 6. If no, deny

6. Has the patient been treated previously with Humira, Kineret or Remicade and therapy is now being switched to Enbrel?
   - If yes, continue to 7. If no, deny

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