

***Title: etanercept (Enbrel)***

<b>Origination:</b> 02/01/06	<b>Revised:</b> 11/11/11	<b>Annual Review:</b> 12/15/11
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**Purpose:**

To provide guidelines and criteria for the review and decision determination of requests for medications that requires prior authorization.

**Background Information:**

***Medication Summary***

- Etanercept is a dimeric fusion protein that binds specifically to tumor necrosis factor (TNF), and blocks interaction with cell surface TNF receptors. Elevated levels of TNF are found in Members with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and plaque psoriasis.
- Etanercept is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in Members with moderately to severely active RA.
- Etanercept is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile rheumatoid arthritis (JRA) in Members who have had an inadequate response to one (1) or more disease modifying anti-rheumatic drugs [medications] (DMARDS).
- Etanercept is indicated for reducing signs and symptoms in Members with active ankylosing spondylitis.
- Etanercept is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in Members with psoriatic arthritis.
- Etanercept is indicated for the treatment of adult Members (18 years or older) with chronic, moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
- Etanercept may be used in combination with methotrexate (MTX) in Members who do not respond adequately to MTX monotherapy.

***Reference Statement***

- Guidelines will be compiled from available US Food and Drug Administration (FDA) approved indications, general practice guidelines, and/or evidence-based uses established through phase III clinical studies without published conflicting data. Only clinical studies published in their entirety in reputable peer-reviewed journals will be evaluated.

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**Background Information, continued:**

***Eligibility Criteria***

- Member must be eligible and have applicable benefits.
- Prior authorization requests that do not meet clinical criteria in this Procedure will be forwarded to a Clinical Pharmacist for review.

***Exclusions***

- Member less than two (2) years of age.
- Concurrent use of multiple biological response modifiers including, but not limited to: Kineret (anakinra), Humira (adalimumab), Cimzia (certolizumab), Amevive (alefacept), and Remicade (infliximab). Only one (1) agent at a time will be covered for the treatment of rheumatoid arthritis, polyarticular juvenile rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, or plaque psoriasis.
- Guttate, erythrodermic, or pustular psoriasis.
- Member experiencing acute infection or significant chronic infection including, but not limited to, sepsis, tuberculosis, aplastic anemia, opportunistic infections.

**Procedure:**

- 1.0 Request for *initial therapy* with etanercept (Enbrel) for **rheumatoid arthritis (RA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
  - 1.1 Provider is a rheumatologist; **AND**
  - 1.2 Member is at least 18 years of age; **AND**
  - 1.3 Diagnosis of moderate to severely active RA as evidenced by at least one (1) of the following:
    - 1.3.1 Swollen and/or tender joints;
    - 1.3.2 Erythrocyte sedimentation rate (ESR)  $\geq$  28mm/hr;
    - 1.3.3 C-reactive protein (CRP)  $\geq$  2.0mg/dL;
    - 1.3.4 Morning stiffness;
    - 1.3.5 Synovitis; **AND**
  - 1.4 Member shows inadequate response to a three (3) to six (6) month minimum trial of an adequate dose of Methotrexate; **OR**

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**Procedure, continued:**

- 1.0 Request for *initial therapy* with etanercept (Enbrel) for **rheumatoid arthritis (RA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following, continued:
  - 1.4 Member has contraindication to Methotrexate as evidenced by **at least one (1)** of the following:
    - 1.4.1 Chronic liver disease;
    - 1.4.2 Leukopenia;
    - 1.4.3 Thrombocytopenia;
    - 1.4.4 Creatinine clearance less than 40mL/minute;
    - 1.4.5 Immunodeficiency; **AND**
  - 1.5 Member shows inadequate response to a three (3) to six (6) month minimum trial of an adequate dose of **OR** is not a candidate for any of the following DMARDs:
    - 1.5.1 Oral or Injectable Gold;
    - 1.5.2 Leflunomide (Arava);
    - 1.5.3 Hydroxychloroquine (Plaquenil);
    - 1.5.4 Sulfasalazine (Azulfidine);
    - 1.5.5 Azathioprine (Imuran);
    - 1.5.6 D-Penicillamine;
    - 1.5.7 Cyclosporine; **AND**
  - 1.6 If all criteria are met, initial therapy with etanercept (Enbrel) 50mg weekly or 25mg twice weekly may be approved for up to three (3) months.
- 2.0 Request for *continuation of therapy* beyond initial authorization period for **rheumatoid arthritis (RA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
  - 2.1 Reduction in Member's signs and symptoms of RA (i.e. 20% improvement in painful joint count, ESR, CRP, or morning stiffness); **AND**
  - 2.2 Improvement in physical functioning;
  - 2.3 If all criteria are met, etanercept (Enbrel) 50mg weekly or 25mg twice weekly may be approved for up to one (1) year.

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**Procedure, continued:**

- 3.0 Request for *initial therapy* with etanercept (Enbrel) for **juvenile rheumatoid arthritis (JRA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
  - 3.1 Provider is a rheumatologist; **AND**
  - 3.2 Diagnosis of active JRA as evidenced by:
    - 3.2.1 Swollen joints, typically large weight-bearing joints, such as the knees or ankles;
    - 3.2.2 Limitation of motion as well as pain and/or tenderness; **AND**
  - 3.3 Member is between two (2) and 17 years of age; **AND**
  - 3.4 Member shows inadequate response to a three (3) to six (6) month minimum trial of an adequate dose of methotrexate; **OR**
  - 3.4 Member has a contraindication to methotrexate (as listed in section 1.4); **AND**
  - 3.5 Member shows inadequate response to a three (3) to six (6) month minimum trial of adequate doses of **OR** is not a candidate for any DMARDs (as listed in section 1.5);
  - 3.6 If all criteria are met, initial therapy with etanercept (Enbrel) at a dose of 0.8mg per kg per week up to 50mg weekly may be approved for up to three (3) months.
- 4.0 Request for *continuation of therapy* beyond initial authorization period for **juvenile rheumatoid arthritis (JRA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying there is reduction in Member's signs and symptoms of JRA:
  - 4.1 If all criteria are met, etanercept (Enbrel) at a dose of 0.8mg per kg per week up to 50mg weekly may be approved for up to one (1) year.

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**Procedure, continued:**

- 5.0 Request for *initial therapy* with etanercept (Enbrel) for **ankylosing spondylitis (AS)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
- 5.1 Provider is a rheumatologist; **AND**
  - 5.2 Member is at least 18 years of age; **AND**
  - 5.3 Diagnosis of active **ankylosing spondylitis (AS)** as evidenced by:
    - 5.3.1 Inflammatory back pain (as defined as stiffness and pain that worsens at rest, and improves with exercise); **AND**
    - 5.3.2 Morning stiffness of 45 minutes or longer; **AND**
  - 5.4 Member shows inadequate response to a three (3) month trial of adequate dose of **OR** is not a candidate for at least two (2) non-steroidal anti-inflammatory medications (NSAIDs) including, but not limited to, the following:
    - 5.4.1 diclofenac (with or without misoprostol);
    - 5.4.2 ibuprofen;
    - 5.4.3 indomethacin;
    - 5.4.4 meloxicam;
    - 5.4.5 naproxen;
    - 5.4.6 celecoxib; **AND**
  - 5.5 Member shows an inadequate response to a three (3) to six (6) month trial of an adequate dose of **sulfasalazine (Azulfidine)** if the Member has a component of *peripheral arthritis* defined as pain/inflammation in arms, legs, elbows, wrist, knees, and/or ankles (5.5 is not required for axial arthritis); **OR**
  - 5.5 Member has a contraindication to sulfasalazine as evidenced by at least one (1) of the following:
    - 5.5.1 GI tract obstruction;
    - 5.5.1 Porphyria;
    - 5.5.1 Urinary Tract Obstruction;
    - 5.5.1 Sulfasalazine hypersensitivity;
  - 5.6 If all criteria are met, initial therapy with etanercept (Enbrel) 50mg weekly or 25mg twice weekly may be approved for up to three (3) months.

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**Procedure, continued:**

- 6.0 Request for *continuation of therapy* beyond initial authorization period for **ankylosing spondylitis** requires clinical documentation that there is reduction in Member's signs and symptoms of AS (i.e., 20% improvement in morning stiffness and degree of nocturnal spinal pain):
- 6.1 If all criteria are met, etanercept (Enbrel) 50mg weekly or 25mg twice weekly may be approved for up to one (1) year.
- 7.0 Request for *initial therapy* with etanercept (Enbrel) for **psoriatic arthritis (PsA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:
- 7.1 Provider is a rheumatologist or dermatologist; **AND**
- 7.2 Member is at least 18 years of age; **AND**
- 7.3 Diagnosis of moderate to severe psoriatic arthritis as evidenced by:
- 7.3.1 At least three (3) swollen and three (3) tender joints; **AND**
- 7.3.2 Erythrocyte sedimentation rate (ESR)  $\geq$  28mm/hr; **AND**
- 7.4 Member shows inadequate response to a three (3) month trial of an adequate dose of or is not a candidate for at least one (1) non-steroidal anti-inflammatory medication (NSAIDs) including, but not limited to the following:
- 7.4.1 Diclofenac (with or without misoprostol);
- 7.4.2 Ibuprofen (Motrin);
- 7.4.3 Indomethacin (Indocin);
- 7.4.4 Meloxicam (Mobic);
- 7.4.5 Naproxen (Naprosyn);
- 7.4.6 Celecoxib (Celebrex); **AND**
- 7.5 Member shows inadequate response to a three (3) to six (6) month minimum trial of an adequate dose of or is not a candidate for at least one (1) of the following DMARDs (either alone or in combination):
- 7.5.1 Sulfasalazine (Azulfidine);
- 7.5.2 Leflunomide (Arava);
- 7.5.3 Methotrexate;
- 7.5.4 Cyclosporine;
- 7.6 If all criteria are met, initial therapy with etanercept (Enbrel) 50mg weekly or 25mg twice weekly may be approved for up to three (3) months.

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**Procedure, continued:**

8.0 Request for *continuation of therapy* beyond initial authorization period for **psoriatic arthritis (PsA)** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying a reduction in Member's signs and symptoms of PsA (i.e., improvement in tender/swollen joint count or ESR level) and/or an improvement in Member's physical functioning:

8.1 If all criteria are met, etanercept (Enbrel) 50mg weekly or 25mg twice weekly may be approved for up to one (1) year.

9.0 Request for *initial therapy* with etanercept (Enbrel) for **plaque psoriasis** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following:

9.1 Provider is a dermatologist; **AND**

9.2 Member is at least 18 years of age; **AND**

9.3 Diagnosis of moderate to severe plaque psoriasis as evidenced by **at least one (1)** of the following:

9.3.1 Involvement of at least 10% of the body surface area (BSA); **OR**

9.3.1 Psoriasis Area and Severity Index (PASI) Score of 10 or greater; **OR**

9.3.1 Psoriasis leading to incapacitation due to plaque location (i.e., head and neck, palms, soles, or genitalia);

**AND**

9.4 Member shows inadequate response to a three (3) to six (6) month minimum trial of **OR** is not a candidate for any of the following topical agents:

9.4.1 Anthralin;

9.4.2 Coal Tar Preparations;

9.4.3 Corticosteroids;

9.4.4 Emollients;

9.4.5 Immunosuppressives;

9.4.6 Keratolytics;

9.4.7 Retinoic Acid Derivatives;

9.4.8 Vitamin D Analogues;

**AND**

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**Procedure, continued:**

- 9.0 Request for *initial therapy* with etanercept (Enbrel) for **plaque psoriasis** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying the following, continued:
- 9.5 Member shows inadequate response to three (3) to six (6) month minimum trial of an adequate dose of **OR** is not a candidate for **at least one (1)** of the following systemic agents:
- 9.5.1 Immunosuppressives;
  - 9.5.1 Retinoic Acid Derivatives;
  - 9.5.1 Methotrexate;
- AND**
- 9.6 Member shows inadequate response to three (3) month to six (6) month minimum trial of **OR** is not a candidate for treatment with phototherapy (PUVA);
- 9.7 If all criteria are met, initial therapy with etanercept (Enbrel) **50mg twice weekly** may be approved for up to three (3) months.
- 10.0 Request for *continuation of therapy* beyond initial authorization period for **plaque psoriasis** requires documentation from the Member's medical records maintained by the requesting independent practitioner verifying a reduction in Member's signs and symptoms (i.e., improvement in body surface area affected, skin lesions and/or PASI score):
- 10.1 If all criteria are met, etanercept (Enbrel) **50mg once weekly or 25mg twice weekly (maintenance therapy)** may be approved for up to one (1) year.

**References:**

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6. Gorman, J. et al. Treatment of Ankylosing Spondylitis By Inhibition of Tumor Necrosis Factor  $\alpha$ . *N Engl J Med*. 2002;346:1349-1356.
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8. Kyle, S. et al. Guideline For Anti-TNF Therapy In Psoriatic Arthritis. *Rheumatology*. 2005;44:390-397.
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10. Mease, P. et al. Etanercept in the Treatment of Psoriatic Arthritis and Psoriasis: A Randomized Trial. *Lancet*. 2000;356:385-90.
11. Moreland, L. et al. Etanercept Therapy in Rheumatoid Arthritis. *Ann Intern Med*. 1999;130:478-486.

**Disclaimer Information:**

Prior Authorization criteria are developed to determine coverage for AvMed Health Plans' benefits, and are published to provide a better understanding of the basis upon which coverage decisions are made. AvMed Health Plans makes coverage decisions based on the Member's benefit plan contract and these criteria. This guideline sets forth concise clinical coverage criteria which have been developed from a review of current literature, policies of the FDA and other government agencies, and other appropriate references, in consultation and with approval from practicing physicians who are members of AvMed's Pharmacy and Therapeutic committee. Treating providers are solely responsible for the medical advice and treatment of Members. This guideline may be updated and therefore is subject to change. The use of these criteria is neither a guarantee of payment nor a final prediction of how specific claim(s) will be adjudicated.