

## Policies Repository



**Policy Title** Etanercept (Enbrel®)

**Policy Number** FS.CLIN.54

*Application of Pharmacy Policy is determined by benefits and contracts. Benefits may vary based on product line, group or contract. Some medications may be subject to precertification, age, gender or quantity edits. Individual member benefits must be verified.*

*This Pharmacy Policy document describes the status of pharmaceutical information and/or technology at the time the document was developed. Since that time, new information relating to drug efficacy, interactions, contraindications, dosage, administration routes, safety or FDA approval may have changed. If the Medical/Pharmacy Reviewer is aware of any new information on the subject of this document, please provide it promptly to the Medical/Pharmacy Policy Department. This information may include new FDA approved indications, withdrawals or other FDA alerts. This type of information is relevant not only when considering whether this Policy should be updated, but also when applying it to current requests for coverage.*

*Members are advised to use participating pharmacies in order to receive the highest level of benefits.*

**Policy**

**Etanercept (Enbrel®)** is indicated for the treatment of moderate to severe rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, moderate to severe juvenile idiopathic arthritis (JIA) and moderate to severe plaque psoriasis.

The use of etanercept (Enbrel®) requires prior authorization (ie, clinical pharmacy and/or Medical Director review).

**Policy Description**

**Etanercept (Enbrel®)** is a biologic agent, a dimeric fusion protein that consists of the extracellular ligand-binding portion of the human tumor necrosis factor (TNF) receptor linked to human immunoglobulin G1 (IgG1). TNF is a naturally occurring protein in the human body that is involved in normal inflammatory and immune responses. Etanercept (Enbrel®) reduces disease activity by binding specifically to TNF and limiting its inflammatory activity in the body. By reducing TNF to normal levels, etanercept (Enbrel®) has been shown to produce symptomatic relief in individuals.

**Policy Guideline Inclusion**

**Etanercept (Enbrel®)** is approved when **any** of the following inclusion criteria is met:

- Documentation of a diagnosis of moderate to severe Rheumatoid Arthritis, Ankylosing Spondylitis or Psoriatic Arthritis and ALL of the following:
  - Patient is an adult ( $\geq$  18 years)
  - Medication is being recommended and prescribed by a rheumatologist
  - Patient had at least a 30 day trial and failure with ONE of the following disease-modifying anti-rheumatic drugs (DMARDs) OR contraindication to ALL of the following DMARDs:
    - Methotrexate

- Hydroxychloroquine
    - Leflunomide
    - Azathioprine
    - Sulfasalazine
    - Adalimumab (Humira®)
  - Patient is not on concurrent therapy with Anakinra (Kineret®) or other tumor necrosis factor antagonists
  - Patient does not have active infections or sepsis
  - Patient has been evaluated (i.e. tuberculin skin test) and does not have active or latent tuberculosis
  - Patient does not have active malignancy
- Documentation of a diagnosis of moderate to severe Juvenile Idiopathic Arthritis (JIA) and ALL of the following:
  - Patient is  $\geq 2$  years old
  - Medication is being recommended and prescribed by a rheumatologist
  - Patient had at least a 30 day trial and failure with ONE of the following disease-modifying anti-rheumatic drugs (DMARDs) OR contraindication to ALL of the following DMARDs:
    - Methotrexate
    - Hydroxychloroquine
    - Leflunomide
    - Azathioprine
    - Sulfasalazine
    - Adalimumab (Humira®)
  - Patient is not on concurrent therapy with Anakinra (Kineret®) or other tumor necrosis factor antagonists
  - Patient does not have active infections or sepsis
  - Patient has been evaluated (i.e. tuberculin skin test) and does not have active or latent tuberculosis
  - Patient does not have active malignancy
- Documentation of a diagnosis of moderate to severe chronic Plaque Psoriasis and ALL of the following:
  - Patient is an adult ( $\geq 18$  years)
  - Medication is being recommended and prescribed by a dermatologist
  - Patient had at least a 30 day trial and failure with ONE of the following drugs OR contraindication to ALL of the following drugs:
    - Topical Calcipotriene containing products
    - Topical Anthralin
    - Topical Steroids
    - Topical immunomodulators (Elidel®, Protopic®)
    - Topical retinoids
    - Efudex
    - Adalimumab (Humira®)
  - Patient is not on concurrent therapy with Anakinra (Kineret®) or other tumor necrosis factor antagonists
  - Patient does not have active infections or sepsis
  - Patient has been evaluated (i.e. tuberculin skin test) and does not have active or latent tuberculosis

- Patient does not have active malignancy

### Policy Guideline Exclusion

For a diagnosis of moderate to severe Rheumatoid Arthritis, Ankylosing Spondylitis or Psoriatic Arthritis, **Etanercept (Enbrel®)** is denied when **any** of the following exclusion criteria is present:

- Patient is less than 18 years old
- Medication is not being prescribed by a rheumatologist
- Patient does not have at least a 30 day trial and failure with ONE of the following disease-modifying anti-rheumatic drugs (DMARDs) or contraindication to ALL of the following DMARDs:
  - Methotrexate
  - Hydroxychloroquine
  - Leflunomide
  - Azathioprine
  - Sulfasalazine
  - Adalimumab (Humira®)
- Patient is on concurrent therapy with Anakinra (Kineret®) or other tumor necrosis factor antagonists
- Patient has active infections or sepsis
- Patient has not been evaluated using tuberculin skin test
- Patient has active or latent tuberculosis
- Patient has active malignancy

For a diagnosis of moderate to severe Juvenile Idiopathic Arthritis (JIA), **Etanercept (Enbrel®)** is denied when **any** of the following exclusion criteria is present:

- Patient is less than 2 years old
- Medication is not being prescribed by a rheumatologist
- Patient does not have at least a 30 day trial and failure with ONE of the following disease-modifying anti-rheumatic drugs (DMARDs) or contraindication to ALL of the following DMARDs:
  - Methotrexate
  - Hydroxychloroquine
  - Leflunomide
  - Azathioprine
  - Sulfasalazine
  - Adalimumab (Humira®)
- Patient is on concurrent therapy with Anakinra (Kineret®) or other tumor necrosis factor antagonists
- Patient has active infections or sepsis
- Patient has not been evaluated using tuberculin skin test
- Patient has active or latent tuberculosis
- Patient has active malignancy

For a diagnosis of moderate to severe chronic Plaque Psoriasis, **Etanercept (Enbrel®)** is denied when **any** of the following exclusion criteria is present:

- Patient is less than 18 years old
- Medication is not being prescribed by a dermatologist
- Patient does not have at least a 30 day trial and failure with ONE of

the following drugs OR contraindication to ALL of the following drugs:

- Topical Calcipotriene containing products
- Topical Anthralin
- Topical Steroids
- Topical immunomodulators (Elidel®, Protopic®)
- Topical retinoids
- Efudex
- Adalimumab (Humira®)
- Patient is on concurrent therapy with Anakinra (Kineret®) or other tumor necrosis factor antagonists
- Patient has active infections or sepsis
- Patient has not been evaluated using tuberculin skin test
- Patient has active or latent tuberculosis
- Patient has active malignancy

#### Policy List of Applicable Drugs

Brand Name	Generic Name
Enbrel	Etanercept

#### Dosing and Administration

Refer to the specific manufacturer's prescribing information for administration and dosage details, contraindications, and Black Box warnings.

#### Policy References

Abouafia DM, Bundow D, Wilske K, et al: Etanercept for the treatment of human immunodeficiency virus- associated psoriatic arthritis. Mayo Clin Proc 2000; 75:1093-1098.

American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 update. [American College of Rheumatology Web site]. Available at: <http://www.rheumatology.org/publications/guidelines/raguidelines02.asp?aud=mem>. [Link is no longer active]

American Thoracic Society, Centers for Disease Control and Prevention. Targeted tuberculin testing and treatment of latent tuberculosis infection. Am J Respir Crit Care Med. 2000;161:S221-S247.

Barrera P, Joosten LA, den Broeder AA, et al: Effects of treatment with a fully human anti-tumour necrosis factor alpha monoclonal antibody on the local and systemic homeostasis of interleukin 1 and TNFalpha in patients with rheumatoid arthritis. Ann Rheum Dis 2001; 60:660-669.

Bos JD, Hagenars C, Das PK, et al. Predominance of "memory" T cells (CD4+, CDw29+) over "naïve" T cells (CD4+, CD45R+) in both normal and diseased human skin. Arch Dermatol Res 1989; 281:24-30.

Bresnihan B, Alvaro-Gracia JM, Cobby M, et al. Treatment of rheumatoid arthritis with recombinant human interleukin-1 receptor antagonist. Arthritis Rheum. 1998; 41:2196-2204.

Deleuran BW, Shu CQ, Field M, et al. Localization of interleukin-1 alpha, type 1 interleukin-1 receptor and interleukin-1 receptor antagonist in the synovial membrane and cartilage/pannus junction in rheumatoid arthritis. Br J Rheumatol. 1992; 31:801-809.

Donahue KE, Gartlehner G, Jonas DE, Lux LJ, Thieda P, Jonas B, Hansen RA,

Morgan LC, Williams SC, Lohr KN. Comparative Effectiveness of Drug Therapy for Rheumatoid Arthritis and Psoriatic Arthritis in Adults. Comparative Effectiveness Review No. 11. (Prepared by RTI-University of North Carolina Evidence-based Practice Center under Contract No. 290-02-0016.) Rockville, MD: Agency for Healthcare Research and Quality. November 2007. Available at: <http://derp.ohsu.edu/about/final-products.cfm>. [Link is no longer active]

Dorner, T, Rumberger, G. The role of B-cells in rheumatoid arthritis: mechanisms and therapeutic targets. *Curr Op Rheum* 2003;15:246-52.

Elliott MJ, Maini RN, Feldmann M, et al. Randomised double-blind comparison of chimeric monoclonal antibody to tumour necrosis factor alpha (cA2) vs. placebo in rheumatoid arthritis. *Lancet*. 1994;344(8930):1105-1110.

Ellis C, Krueger GG. Treatment of chronic plaque psoriasis by selective targeting of memory effector T lymphocytes. *N Engl J Med* 2001; 345:248-255.

Enbrel<sup>®</sup> (Etanercept) In: Facts and Comparisons [online through Facts and Comparisons Online]. Indy, IN: Walter Kluwer Health Inc. Accessed September 9, 2010.

Enbrel<sup>®</sup> (Etanercept) In: Drugdex [online through Micromedex Healthcare Series]. Greenwood Village, CO: Thomson Micromedex. Accessed September 9, 2010.

Enbrel<sup>®</sup> (Etanercept) [package insert]. Thousand Oaks, CA: Immunex Corporation; 2007.

Finckh A, Simard JF, Duryea J, Liang MH, Huang J, Daneel S, et al. The effectiveness of anti-tumor necrosis factor therapy in preventing progressive radiographic joint damage in rheumatoid arthritis: a population-based study. *Arthritis Rheum* 2006;54(1):54-9.

Firestein GS, Boyle DL, Yu C, et al. Synovial interleukin-1 receptor antagonist and interleukin-1 balance in rheumatoid arthritis. *Arthritis Rheum*. 1994; 37:644-652.

Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. *Arthritis Rheum*. 1980;23(2):137-145.

Gartlehner G, Hansen RA, Thieda P, Jonas B, Lohr KN, Carey T. Drug Class Review on Targeted Immunomodulators [Final Report] January 2007. Oregon Health & Science University. Drug Effectiveness Review Project [available at <http://derp.ohsu.edu/about/final-products.cfm>]. Accessed July 1, 2009. [Link is no longer active]

Genant HK, Jiang Y, Peterfy C, Lu Y, Re´dei J, Countryman PJ. Assessment of rheumatoid arthritis using a modified scoring method on digitized and original radiographs. *Arthritis Rheum*. 1998;41(9):1583-1590.

Gladman DD. Traditional and newer therapeutic options for psoriatic

arthritis: an evidence-based review. *Drugs* 2005;65(9):1223-38.

Gorman JD, Sack KE, & Davis JC Jr: Treatment of ankylosing spondylitis by inhibition of tumor necrosis factor alpha. *N Engl J Med* 2002; 346(18):1349-1356.

Iyer S, Yamauchi P, & Lowe NJ: Etanercept for severe psoriasis and psoriatic arthritis: observations on combination therapy. *Brit J Dermatol* 2002; 146:118-121.

Johnson CJ, Reilly KM, & Murray KM: Etanercept in juvenile rheumatoid arthritis. *Ann Pharmacother* 2001; 35:464-471.

Kavanaugh AF, Ritchlin CT. Systematic review of treatments for psoriatic arthritis: an evidence based approach and basis for treatment guidelines. *J Rheumatol* 2006;33(7):1417-21.

Khanna D, Liebling MR, & Louie JS: Etanercept ameliorates sarcoidosis arthritis and skin disease. *J Rheumatol* 2003; 30:1864-1867.

Leonardi CL, Powers JL, Matheson RT, et al: Etanercept as monotherapy in patients with psoriasis. *N Engl J Med* 2003; 349(21):2014-2022.

Mease PJ, Goffe BS, Metz J, et al: Etanercept in the treatment of psoriatic arthritis and psoriasis: a randomised, trial. *Lancet* 2000; 356:385-390.

National Institute for Clinical Excellence (NICE). A systematic review of the effectiveness of adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis in adults and an economic evaluation of their cost-effectiveness. London (UK): National Institute for Clinical Excellence (NICE); October 2005.

Pincus T, Summey JA, Soraci SA Jr, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified Stanford Health Assessment Questionnaire. *Arthritis Rheum.* 1983;26(11):1346-1353.

Ries LAG, Eisner MP, Kosary CL, Hankey BF, Miller BA, Clegg L, Mariotto A, Feuer EF, Edwards BK (eds). SEER Cancer Statistics Review, 1975-2001, National Cancer Institute. Bethesda, MD, [http://seer.cancer.gov/csr/1975\\_2001/](http://seer.cancer.gov/csr/1975_2001/). Accessed September 9, 2010.

Sandborn WJ, Hanauer SB, Katz S, et al: Etanercept for active Crohn's disease: a randomized, double-blind, placebo-controlled trial. *Gastroenterology* 2001; 121:1088-1094.

Scallon BJ, Moore MA, Trinh H, et al. Chimeric anti-TNF $\alpha$  monoclonal antibody cA2 binds recombinant transmembrane TNF $\alpha$  and activates immune effector functions. *Cytokine.* 1995;7:251-259.

Takei S, Groh D, Bernstein B, et al: Safety and efficacy of high dose etanercept in treatment of juvenile rheumatoid arthritis. *J Rheumatol* 2001; 28(7):1677-1680.

Van der Heijde D, DaSilva JC, Dougados M, et al: Once-weekly 50-mg dosing of Etanercept (Enbrel(R)) is as effective as 25-mg twice-weekly dosing in patients with ankylosing spondylitis. *Ann Rheum Dis* 2006; online:09/12/06.

Van der Heijde DM, van Leeuwen MA, van Riel PL, et al. Biannual radiographic assessments of hands and feet in a three-year prospective follow-up of patients with early rheumatoid arthritis. *Arthritis Rheum.* 1992;35(1):26-34.

Van der Linden S, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. A proposal for modification of the New York criteria. *Arthritis Rheum.* 1984;27(4):361-368.

Ware JE Jr, Gandek B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. *J Clin Epidemiol.* 1998;51(11):903-912.

Weinblatt ME, Kremer JM, Bankhurst AD, et al: A trial of etanercept, a recombinant tumor necrosis factor receptor:Fc fusion protein, in patients with rheumatoid arthritis receiving methotrexate. *N Engl J Med* 1999; 340 (4):253-259.

Weisman M, Keystone E, Paulus H, et al: A dose escalation study designed to demonstrate the safety, tolerability and efficacy of the fully human anti-TNF antibody, D2E7, given in combination with methotrexate (MTX) in patients with active RA (abstract 1948). *Arthritis Rheum* 2000; 43(9 Suppl S):S391.

---

#### Policy Link to Related Policies

---

Printed 10/13/2010 09:26:51

---

The Policy Bulletins on this web site were developed to assist Independence Blue Cross and its subsidiaries ("IBC") in administering the provisions of the respective benefit programs, and do not constitute a contract. If you are an IBC member, please refer to your specific benefit program for the terms, conditions, limitations and exclusions of your coverage. IBC does not provide health care services, medical advice or treatment, or guarantee the outcome or results of any medical services/treatments. The facility and professional providers are responsible for providing medical advice and treatment. Facility and professional providers are independent contractors and are not employees or agents of IBC. If you have a specific medical condition, please consult with your doctor. IBC reserves the right at any time to change or update its Policy Bulletins. © 2008 Independence Blue Cross. All Rights Reserved. Current Procedural Terminology © 2008 American Medical Association. All Rights Reserved.