MEDICAL POLICY STATEMENT		
Effective Date	**Next Annual Review Date**	**Last Review / Revision Date**
06/15/2011	**06/15/2012**	**06/15/2011**
Author		
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CSMG Medical Policy Statements are derived from literature based and supported clinical guidelines, nationally recognized utilization and technology assessment guidelines, other medical management industry standards, and published MCO clinical policy guidelines. Medically necessary services are those health care services or supplies which are proper and necessary for the diagnosis or treatment of disease, illness, or injury and without which the patient can be expected to suffer prolonged, increased or new morbidity, impairment of function, dysfunction of a body organ or part or significant pain and discomfort. These services meet the standards of good medical practice in the local area, are the lowest cost alternative and are not provided mainly for the convenience of the member or provider.

A. SUBJECT

Etanercept (Enbrel) Injection

B. BACKGROUND

Etanercept (Enbrel) is a dimeric soluble form of the p75 TNF receptor that can bind TNF molecules. Etanercept (Enbrel) inhibits binding of TNF-a and TNF-b (lymphotoxin alpha [LT-a]) to cell surface TNFRs, rendering TNF biologically inactive. In *in vitro* studies, large complexes of etanercept (Enbrel) with TNF-a were not detected and cells expressing transmembrane TNF that binds etanercept (Enbrel) are not lysed in the presence or absence of complement. Etanercept (Enbrel) can modulate biological responses that are induced or regulated by TNF, including expression of adhesion molecules responsible for leukocyte migration (eg, E-selectin, and to a lesser extent, intercellular adhesion molecule-1[ICAM-1]), serum levels of cytokines (eg, IL-6), and serum levels of matrix metalloproteinase-3 (MMP-3 or stromelysin).

The patient selection criteria outlined was derived from the FDA-approved prescribing information for etanercept (Enbrel), the studies that were presented to the FDA in support of the pre-market approval application, and studies in the peer-reviewed published medical literature. The FDA label indications found in the manufacturer prescribing information and described below are rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis and plaque psoriasis. Coverage decisions for conditions other than the above FDA-approved indications will be reviewed on a case-by-case basis if proven effective through research documentation. The requesting provider will need to support his exception request with the appropriate literature.

C. POLICY

CareSource will approve the use of etanercept (Enbrel), and consider its use as medically necessary when the following criteria have been met for:

- Rheumatoid arthritis
- Juvenile Idiopathic Arthritis
- Ankylosing Spondylitis

- Psoriatic Arthritis
- Plaque Psoriasis

CareSource will approve the use of etanercept (Enbrel), and consider its use as medically necessary for the following off label uses:

- Graft vs host
- Hidradentitis Suppurativa
- Bechets

Etanercept (Enbrel) is considered investigational and not covered for the treatment of:

- Congestive heart failure
- Crohn's
- Nephrotic Syndrome
- Pyoderma Gangrenosum
- Uveitis
- Wegener Granulomatosis

Rheumatoid Arthritis

Etanercept (Enbrel) is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severe active rheumatoid arthritis who have had a documented inadequate response to single therapy or inability to tolerate the DMARD (disease-modifying anti-inflammatory drugs).

Prior Authorization Criteria:

- Documented diagnosis of moderate to severe active rheumatoid arthritis.
- Prescribed by a rheumatologist or under recommendation of rheumatologist.
- Failure of a trial of one DMARD

OR

- Unable to tolerate or has a medical contraindication of conventional therapies

Etanercept can be used alone or in combination with methotrexate

Juvenile Idiopathic Arthritis (formerly known as Juvenile Rheumatoid Arthritis)

Etanercept (Enbrel) is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older.

Prior Authorization Criteria:

- Documented diagnosis of active moderate to severe polyarticular juvenile idiopathic arthritis
- Prescribed by a rheumatologist or under recommendation of rheumatologist
- Failure of a trial of one DMARD

OR

- Unable to tolerate or has a medical contraindication of conventional therapies

Ankylosing Spondylitis

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

Prior Authorization Criteria:

- Documented diagnosis of active ankylosing spondylitis
- Prescribed by a rheumatologist or under recommendation of rheumatologist
- BASDI (Bath anklyosing spondylitis disease activity index) score of greater than or equal to 4. (www.Spondylitis.org and www.asas-group.org)
- Failure of at least one non-biological DMARD in patients without pure axial disease. If pure axial disease, no requirement for DMARD failure

  OR
- Unable to tolerate conventional or has medical contraindication to conventional therapies

Psoriatic Arthritis

Etanercept (Enbrel) is indicated for reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in patients with psoriatic arthritis.

Prior Authorization Criteria:

- Documented diagnosis of active psoriatic arthritis
- Failure of a trial of at least one non-biological DMARD

  OR
- Unable to tolerate or has a medical contraindication of conventional therapies

Note: Documentation of an inadequate response to a non-biological DMARD is *NOT* necessary if the intention is to administer these with etanercept (Enbrel). A trial should be attempted of a DMARD alone before adding etanercept (Enbrel) as combination therapy.

Plaque Psoriasis

Etanercept (Enbrel) is indicated for the treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate for adult patients 8 years and older.

Prior Authorization Criteria:

- Documented diagnosis of moderate to severe plaque type psoriasis
  - Psoriatic plaques covering at least 7-8% of the body surface area or involvement with critical areas (hands, feet, faces or genitals)
- Failure of prior treatment with psoralen-UVA or UVB

OR

- Failure of a trial of other systemic therapies, such as:
  - Methotrexate
  - Cyclosporine (Neoral, Sandimmune, Gengraf)
  - Acitretin (Soriatane)

NOTE: Psoriasis patients should be monitored for non-melanoma skin cancers (NMSCs), particularly those patients who have had prior prolonged phototherapy treatment.

NOTE: Documented diagnosis must be confirmed by portions of the individual's medical record, which will confirm the presence of disease and will need to be supplied with prior authorization request. These medical records may include, but not limited to test reports, chart notes from provider's office or hospital admission notes.

For Special Needs Plan members, reference the below link to search for Applicable National Coverage Descriptions (NCD) and Local Coverage Descriptions (LCD):

For Medicare

NCD for etanercept (Enbrel) Injection

Medicare does not have a National Coverage Determination (NCD) for etanercept (Enbrel) Injection. In general, Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. Refer to the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, section 50 Drugs and Biologicals at:

http://www.cms.hhs.gov/manuals/Downloads/bp102c15.pdf.

Local Coverage Determinations (LCDs) for etanercept (Enbrel**)** do not exist at this time. (Accessed February 16, 2011)

Safety

CareSource will only review requests for **etanercept (Enbrel)** if the patient has **none** of the following contraindications:

- Patient has hypersensitivity to etanercept
- Patient has Tuberculosis (active, untreated or reactivation of latent TB), or contact with person with active TB or traveled to countries with high incidence of TB, or other active serious infections, or a history of recurrent infections including invasive fungal infections, bacterial, viral and other infections caused by opportunistic pathogens, or has other respiratory disorders including Chronic Obstructive Pulmonary Disease (COPD)
- Patient has not had a tuberculin skin test (TST), or a CDC-recommended equivalent, to rule out latent tuberculosis
- Patient is positive for hepatitis B during therapy or there is evidence of no recovery from prior hepatitis B infection
- Patient is not up to date with all immunizations in agreement with current immunization guidelines prior to initiating the therapy (patient may not be given live vaccines

concurrently with adalimumab, and the interval between vaccination and initiation of adalimumab therapy must in accordance with current vaccination guidelines)
- Has sepsis
- Patient is going to have concurrent use with tumor necrosis factor antagonists or anakinra (Kineret) and/or TNF blockers
- Currently taking cyclophosphamide or sulfasalazine
- Treatment is being initiated in a patient with moderate to severe heart failure. The clinician will need to evaluate risk vs benefits of treatment
- Patient has a diagnosis of Lymphoma and other malignancies
- Is at risk for opportunistic infections

Pregnancy Risk Factor = B
There are no studies in pregnant women. Although the human pregnancy experience is very limited, there is no evidence of embryofetal harm. However, the human data are too limited for an assessment of the risk. Use this drug during pregnancy only if clearly needed.

It is not known whether etanercept (Enbrel) is excreted in human milk or absorbed systemically after ingestion. Because etanercept (Enbrel) is a protein, it most likely would be digested in the infant's stomach and not absorbed systemically. Because many drugs and immunoglobulins are excreted in human milk, and because of the potential for serious adverse reactions from etanercept (Enbrel) in breastfeeding infants, decide whether to discontinue breastfeeding or the drug.

Conditions of Coverage

Quantity Limitations	200mg per month Plaque Psoriasis – 400mg for the first 3 months, then 200mg per month Juvenile Rheumatoid Arthritis – 0.8mg/kg up to 50mg/week (200mg per month)
J-Code	J1438
NDC	58406045501 58406045504 54868478200 58406042534 58406042541 54868544400 58406043501 58406043504 58406044501 58406044504
Applicable ICD-9 Code	279.50 Graft vs. Host Disease 705.83 Hidradenitis Suppurativa 136.1 Behcet's 696.0 Psoriatic arthropathy

	696.1	Other psoriasis [moderate to severe chronic plaque psoriasis]
	714.0 714.2	Rheumatoid arthritis [moderately to severely active in adults]
	714.30 714.33	Juvenile chronic polyarthritis [severely active]
	720.0	Ankylosing spondylitis
Place Of Service	Office, Outpatient, Home *****Preferred place of service is in the home*.** **Note:** CareSource supports administering injectable medications in various settings, as long as those services are furnished in the most appropriate and cost-effective setting that are supportive of the patient's medical condition and unique needs and condition. The decision on the most appropriate setting for administration is based on the member's current medical condition and any required monitoring or additional services that may coincide with the delivery of the specific medication.	
Authorization Period	Approved initial authorizations are valid for 3 months. Continued treatment may be considered when the member has shown biological response to treatment. All authorizations are subject to continued eligibility.	

D. REVIEW / REVISION HISTORY

6/15/2011

E. REFERENCES

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The medical Policy Statement detailed above has received due consideration as defined in the Medical Policy Statement Policy and is approved.

June 2, 2011

Chief Medical Officer **Date**

June 2, 2011

Senior Medical Director **Date**