Pharmacy Management Drug Policy

SUBJECT: Enbrel® (etanercept) – for Ankylosing Spondylitis, Juvenile Idiopathic Arthritis, Plaque Psoriasis, Psoriatic Arthritis and Rheumatoid Arthritis
POLICY NUMBER: Pharmacy-13
EFFECTIVE DATE: 5/09
LAST REVIEW DATE: 12/4/2019

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Enbrel® (Etanercept) binds specifically to TNF and blocks its interaction with cell-surface tumor necrosis factor receptors (TNFRs). TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses.

Enbrel® is indicated for:

- reducing the signs and symptoms in patients with active ankylosing spondylitis
- the treatment of adult & pediatric patients 4 years of age and older with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy
- reducing the signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients 2 years of age and older
- reducing the signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis.
- reducing the signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active RA

POLICY:

Based upon our assessment and review of the peer-reviewed literature Enbrel® has been medically proven to be effective and therefore, **medically necessary** for the treatment of the following diagnoses if specific criteria are met:

I. Ankylosing Spondylitis

a. Member must be actively followed by and the drug prescribed by a Rheumatologist
b. Member must have ankylosing spondylitis
c. Presence of refractory disease defined by failure of at least two different prescription strength NSAIDS at maximum dose for at least 1 month each
d. Approved dosing is 50mg/week

II. Juvenile Idiopathic Arthritis

a. Member must be actively followed by a Rheumatologist **AND**
b. Member must be at least 2 years old **AND**
c. Member must have moderately to severely active polyarticular juvenile idiopathic arthritis **AND**
d. Member must have failed to respond to and/or is intolerant to approved disease-modifying antirheumatic drugs (DMARDs) agents, such as methotrexate, NSAIDs, analgesics or corticosteroids either alone or in combination
e. The recommended dose for pediatric patients ages 2 to 17 years with active polyarticular-course JRA is 0.8mg/kg per week up to a maximum of 50mg per week

III. Plaque Psoriasis

A. Enbrel is medically appropriate if **all** of the following are met:

1. Member must be followed by a dermatologist or rheumatologist

2. Member must be at least 4 years of age

3. Member must have moderate to severe chronic plaque psoriasis that involves at least 10% of their body surface area (BSA). Consideration will be given to those who have severe disease of the hands or feet or other areas causing disruption in normal activities, but have less than 10% BSA involvement. **AND**

4. Member must be a candidate for systemic therapy, i.e. Acitretin, methotrexate, or cyclosporine with a trial period of at least 3 months. If contraindications (medical reason to avoid the drug) are present or had developed serious side effects to the above mentioned agents before 3 months, a trial of one of the other three criteria listed below must be present **OR**

5. If member does not qualify as stated above in **"4"**, then one of the following must be attempted for a reasonable period of time (at least 3 months):

a. UVB in combination with a topical therapy such as coal tar, steroids or tazarotene **OR**

b. PUVA in combination with topical corticosteroids **OR**

c. Medium/High potency topical steroids in combination with anthralin, calcipotriene, or tazarotene **AND**

6. There must be documentation of drug failure or serious side effects to the preferred alternative: Humira

a. This requirement will be waived for pediatric patients

B. Authorization period and dosing limitations:

1. Adult dosing (age 18 and up):

a. Coverage of Enbrel in psoriasis patients is limited to 50mg twice weekly for the first 3 months, and then maintenance therapy not exceeding doses of 50mg per week

1. Quantity # 8 of 50mg/ 30 days for initial 3 months

2 .Quantity # 4 of 50mg/ 30 days or # 8 of 25mg/ 30 days for maintenance therapy If adequate response is not achieved after 24 weeks, a constant dose of 50 mg twice weekly may be considered.

2. Pediatric Dosing (age 4 – 17)

a. Given as 0.8mg/kg weekly, up to a maximum of 50mg/week

IV. Psoriatic Arthritis

a. A diagnosis of definitive psoriatic arthritis established by a Rheumatologist or Dermatologist **AND**

b. Member must be actively followed by and the drug prescribed by a Rheumatologist or Dermatologist **AND**

c. Member must have some clinical features of psoriatic arthritis such as: involvement of the DIP joints, an asymmetric distribution of joint disease, spondyloarthritis, sausage digits, new bone formation on radiographs, cutaneous findings, and the characteristic nail manifestations of psoriatic arthritis (nail pitting, onycholysis & other lesions, which

include leukonychia, red spots in the lunula, and nail plate crumbling) all may be present

d. Approved dosing is 50mg/week

V. Rheumatoid Arthritis

a. Member must be actively followed by and the drug prescribed by a Rheumatologist **AND**

b. Member must have active moderate to severe rheumatoid arthritis **AND**

c. Member must have failed to respond to and/or is intolerant to approved disease-modifying antirheumatic drug (DMARD) agents, such as methotrexate, azathioprine, sulfasalazine, or hydroxychloroquine, either alone or in combination for a 3 month period **AND**

d. Approved dosing is 50mg per week. Doses higher than 50mg per week are not recommended based on a study of Enbrel 50mg twice weekly in patients with rheumatoid arthritis suggesting a higher incidence of adverse events but similar ACR response rates

e. Low disease activity or remission should be considered treatment targets for members receiving etanercept. Members with moderate or high disease activity >3 months due to lack of or loss of benefit should discontinue etanercept and switch to another biologic agent.

f. Members with high disease activity who fail etanercept therapy due to a serious adverse effect should switch to a non-TNF biologic. Members with moderate or high disease activity who fail etanercept therapy due to non-serious adverse effects should switch to another TNF-blocker or a non-TNF biologic agent.

The following are **non-FDA approved indications** which **may be considered medically appropriate:**

VI. Hidradenitis Suppurativa

a. Member must be actively followed by and drug prescribed by a Dermatologist **AND**

b. Must have a diagnosis of stage II or III severe refractory hidradenitis suppurativa with recurrent abscesses

c. Must have had a minimum of a three month trial of systemic antibiotics (such as minocycline, doxycycline, clindamycin, rifampin) which failed to provide clinical improvement

d. Initial approval will be for 25mg twice a week for 3 months, Continuation of therapy will require documented improvement of disease.

VII. Graft versus Host Disease (Pediatric patients):

a. Member must have moderate (grade 2) to severe (grade 3 to 4) GVHD.

b. The member must be under the age of 18 years old. Adults ages 18 and older will follow the off-label policy criteria for this disease.

c. The member must have failed to respond to conventional immunosuppressive therapy, such as methotrexate, prednisone, tacrolimus and/or cyclosporine.

d. Initial approval will be for 25mg twice a week for 4 weeks, then weekly dosing thereafter for up to 3 months (12 weeks total dosing). Continuation of therapy will require documented improvement of disease.

POLICY GUIDELINES:

1. Prior-authorization is contract dependent.
2. Etanercept is self-administered and therefore falls under the pharmacy benefit.
3. Consideration should be given to initiating therapy with a DMARD such as methotrexate, NSAID, or steroid depending on diagnosis.
4. Involvement of the DIP joints, an asymmetric distribution of joint disease, spondyloarthritis, sausage digits, new bone formation on radiographs, cutaneous findings, and the characteristic nail manifestations of psoriatic arthritis all help to distinguish psoriatic arthritis from other inflammatory arthritis, including RA.
5. Enbrel is **not to be used in immunocompromised patients** due to the possible risk of serious infection.
6. In clinical trials of all TNF inhibitors, a higher rate of lymphoma was seen compared to the general population; however, the risk of lymphoma may be up to several-fold higher in RA and psoriasis patients. Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF- blockers, including etanercept
7. Tuberculosis (frequently disseminated or extrapulmonary at clinical presentation), invasive fungal infections, and other opportunistic infections have been observed in patients receiving Enbrel. All patients being considered for biologic therapy should be screened for latent tuberculosis infection, regardless of the presence of risk factors. Annual testing is recommended for patients who live, travel, or work in situations where tuberculosis exposure is likely.
8. Use of TNF inhibitors has been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic carriers of this virus. Patients at risk for HBV infection should be evaluated for prior evidence of HBV infection before initiating TNF inhibitor therapy. Patients with plaque psoriasis who are seropositive for hepatitis B surface antigen with inactive disease should undergo a course of antiviral therapy 2 – 4 weeks prior to initiation of anti-TNF therapy.
9. Cases of worsening congestive heart failure (CHF) and new onset CHF have been reported with TNF blockers. Exercise caution when using Enbrel in patients who have heart failure and monitor them carefully. Use of anti-TNF agents is not recommended in patients with New York Heart Association class III or IV heart failure who have an ejection fraction of 50% or less
10. Etanercept is considered the agent of choice for RA patients with hepatitis C who require biologic therapy.
11. Patients should not receive live attenuated herpes zoster vaccine while receiving anti-TNF therapy.
12. Etanercept will not be authorized when used in combination with other biologics such as Kineret (anakinra), Orencia (abatacept), Rituxan (rituximab),

UPDATES:

Date:	Revision:
12/19	Review
12/18	Review
12/17	Revision
04/17	Revision
11/16	Revision
03/16	Revision
12/14	Revision
12/13	Revision
10/13	Revision
06/13	Revision
02/13	Revision
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REFERENCES:

1. Psoriasis Symposium. Program of the 61st Annual Meeting of the American Academy of Dermatology; March 22-26, 2003; San Francisco, California.
2. Callan JP, Krueger GG, Lebwohl M, et al. AAD Statement of Psoriasis Therapies. J Am Acad Dermatol. 2003. Nov;49(5): 897-899.
3. Enbrel package insert. Thousand Oaks, CA: Immunex Corp [Amgen]; Revised 11/2016. Accessed 04/2017.
4. Pearce DJ, et al. The cost-effectiveness and cost of treatment failures associated with systemic psoriasis therapies. Journal of Dermatological Treatment. 2006;17:29-37.
5. Gordon KB, et al. Clinical response in psoriasis patients discontinued from and then reinitiated on etanercept therapy. Journal of Dermatological Treatment. 2006;17:9-17.
6. Elewski B, et al. Comparison of clinical and pharmacokinetic profiles of etanercept 25 mg twice weekly and 50 mg once weekly in patients with psoriasis. British Journal of Dermatology 2007 156, pp138–142.
7. Papp KA. The long term efficacy and safety of new biological therapies for psoriasis. Archives of Dermatological Research. June 2006;298(1): 7-15.
8. American College of Rheumatology, Guidelines for the Management of Rheumatoid Arthritis - 2002 Update, Arthritis and Rheumatism, Vol. 46, No.2, February 2002, pg. 328-346.
9. Weinblatt, M et.al. Long-term and phase III treatment of DMARD failing rheumatoid arthritis patients with TNF receptor p75 Fcfusion protein (TNFR:Fc; Enbrel™). Arthritis Rheum 1977; 40(suppl):S126. Abstract 572.
10. Alice Gottlieb, Neil J. Korman, Kenneth B. Gordon, Steven R. Feldman, Mark Lebwohl, John Y.M. Koo, Abby S. Van Voorhees, Craig A. Elmets, Craig L. Leonardi, Karl R. Beutner, Reva Bhushan, Alan Menter Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: Overview and guidelines of care for treatment with an emphasis on the biologics *Journal of the American Academy of Dermatology*, *Volume 58, Issue 5*, *May 2008*, *Pages 851-864*
11. J Am Academy Dermatol *Guidelines of Care for the Management of Psoriasis and Psoriatic Arthritis*; 58: 839, May 2008

12. Arch Dermatology; *Long-term Safety and Efficacy of 50 mg of Etanercept Twice Weekly in Patients with Psoriasis* Volume 143(6):719-726, June 2007
13. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis care & research.* May 2012;64(5):625-639.
14. Hsu S, Papp KA, Lebwohl MG, et al. Consensus guidelines for the management of plaque psoriasis. *Archives of dermatology.* Jan 2012;148(1):95-102
15. Braun J et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;**70**:896–904.
16. Pelekanou A, Kanni T, Savva A, et al. Long-term efficacy of etanercept in hidradenitis suppurativa: results from an open-label phase II prospective trial. *Exp Dermatol.* 2010; 19(6):538.
17. Shuja F, Chan CS, Rosen T. Biologic drugs for the treatment of hidradenitis suppurativa: an evidence-basereview. *Dermatol Clin.* 2010; 28(3):511.
18. Rambhatla PV, Lim HW, Hamzavi I. A systematic review of treatments for hidradenitis suppurativa. *Arch Dermatol.* 2012; 148(4):439.
19. Adams DR, Yankura JA, Fogelberg AC, et al. Treatment of hidradenitis suppurativa with etanercept injection. *Arch Dermatol* 2010; 146(5):501.
20. Andolina M, Rabusin M, Maximova N, et al: Etanercept in graft-versus-host disease (letter). Bone Marrow *Transplant* 2000; 26:929.
21. Chiang KY, Abhyankar S, Bridges K, et al. Recombinant human tumor necrosis factor receptor fusion protein as complementary treatment for chronic graft-versus-host disease. *Transplantation*. 2002;73(4):665
22. Park JH, Lee HJ, Kim SR, et al. Etanercept for steroid-refractory acute graft versus host disease following allogeneic hematopoietic stem cell transplantation. *Korean J Intern Med.* 2014 Sep;29(5):630-6
23. Menter A, Korman N, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Case-based presentations and evidence-based conclusions. *J Am Acad Dermatol* 2011;65: 137-74