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: 05/2009
LAST REVIEW DATE: 08/24/2023

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. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☐ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☐ Dual Eligible Special Needs Plan (D-SNP)	

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

Pharmacy Management Drug Policy
Enbrel (etanercept)

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 JIA is 0.8mg/kg per week up to a maximum of 50mg per week

III. **Plaque Psoriasis**
- a. Enbrel is medically appropriate if **ALL** 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 less than 10% body surface area involvement but have severe disease of sensitive areas or areas causing significant disruption in normal activities (such as the hands, feet, face, genitalia) **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 that resulted in an inadequate response (failure). A 3-month trial will not be required if the member experienced serious side effects during a trial of one of the above-mentioned agents **OR**
  5. If systemic therapy is contraindicated, then one of the following must be attempted for a reasonable period of time (at least 3 months):
     - i. UVB in combination with a topical therapy such as coal tar, steroids or tazarotene **OR**
     - ii. PUVA in combination with topical corticosteroids **OR**
     - iii. Medium/High potency topical steroids in combination with anthralin, calcipotriene, or tazarotene
- b. Authorization period and dosing limitations:
  1. **Adult dosing** (age 18 and up):
     - i. 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
     - ii. 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)
     - i. 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:**
   a. Member must have moderate (grade 2) to severe (grade 3 to 4) GVHD.
   b. The member must have failed to respond to conventional immunosuppressive therapy, such as methotrexate, prednisone, tacrolimus and/or cyclosporine.
   c. 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. Unless otherwise stated above within the approval time period section, approval time periods will be for 1 year
   - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e., generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.
2. Prior authorization is contract dependent.

3. This policy is applicable to drugs that are included on a specific drug formulary. If a drug referenced in this policy is non-formulary, please reference the Non-Formulary Medication Exception Review Policy for all Lines of Business (Pharmacy-69).
4. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
    - The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
    - The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
    - The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
    - The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
    - The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
    - The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.
5. Etanercept is self-administered and therefore falls under the pharmacy benefit.
6. Consideration should be given to initiating therapy with a DMARD such as methotrexate, NSAID, or steroid depending on diagnosis.
7. 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.
8. Enbrel is **not to be used in immunocompromised patients** due to the possible risk of serious infection.
9. 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
10. 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.
11. 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.

12. 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
13. Etanercept is considered the agent of choice for RA patients with hepatitis C who require biologic therapy.
14. Patients should not receive live attenuated herpes zoster vaccine while receiving anti- TNF therapy.
15. **Concurrent use of Inflammatory Agents**
    a. Enbrel as well as other immunomodulating therapies or Targeted Synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) (Stelara, Cimzia, Remicade, biosimilars, etc.) should not be administered in combination with another biologic or targeted synthetic DMARD used for an inflammatory condition. Combination therapy is generally not recommended due to the added risk of immunosuppression, potential for a higher rate of adverse effects, and lack of evidence for additive therapy. NOTE: This does NOT exclude the use of conventional synthetic DMARDs (e.g., MTX, leflunomide, hydroxychloroquine, and sulfasalazine) in combination with biologics and targeted synthetic DMARDs.
    b. Requests for the concurrent use of inflammatory agents will be evaluated for safety and efficacy and are subject to off-label review.
    c. Otezla in combination with biologic DMARD therapy (such as adalimumab, Enbrel, Cosentyx, etc.) is not FDA approved or supported with a high level of clinically valid medical evidence for the treatment of plaque psoriasis or psoriatic arthritis. Therefore, these requests are considered combination therapy and are considered not medically necessary.

UPDATES:

DATE	REVISION
08/24/2023	P&T Committee Approval
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