SPECIALTY GUIDELINE MANAGEMENT

ENBREL® (etanercept)

POLICY

A. INDICATIONS
The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

**FDA-Approved Indications**
- Moderately to severely active rheumatoid arthritis (RA)
- Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)
- Active psoriatic arthritis (PsA)
- Active ankylosing spondylitis (AS)
- Moderate to severe chronic plaque psoriasis (PsO)

**Compendial Uses**
- Axial spondyloarthritis
- Hidradenitis suppurativa
- Reactive arthritis

All other indications are considered experimental/investigational and are not a covered benefit.

B. REQUIRED DOCUMENTATION
The following information is necessary to initiate the prior authorization review:
- Pretreatment tuberculosis (TB) screening with TB skin test or an interferon gamma release assay (e.g., QFT-GIT, T-SPOT.TB) and TB treatment status (if applicable) documented in member’s chart or medical record
  - Members who have received at least a 28-day supply of Enbrel, any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) in a paid claim in a paid claim through a pharmacy or medical benefit within the previous 120 days of the continuation request are exempted from all requirements related to TB screening and treatment in this Policy.

C. EXCLUSIONS
- Untreated latent TB infection
  - Treatment must be initiated prior to starting Enbrel.
- Active tuberculosis infection
  - Treatment must be completed prior to starting Enbrel.

D. CRITERIA FOR APPROVAL
1. Moderately to severely active rheumatoid arthritis (RA)
   a. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Enbrel, any other biologic DMARD or targeted synthetic DMARD (e.g., Xeljanz) indicated for moderately to severely active rheumatoid arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Enbrel.

   b. Authorization of 24 months may be granted for members who meet ANY of the following criteria:
      i. Inadequate response to at least a 3-month trial of methotrexate (MTX) despite adequate dosing (i.e., titrated to 25-30 mg/week)
      ii. Intolerance or contraindication to MTX
Contraindications to MTX – Examples:
- History of intolerance or adverse event
- Alcoholic liver disease or other chronic liver disease
- Elevated liver transaminases
- Interstitial pneumonitis or clinically significant pulmonary fibrosis
- Renal impairment
- Pregnancy or planning pregnancy (male or female)
- Breastfeeding
- Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
- Myelodysplasia
- Hypersensitivity
- Significant drug interaction

iii. Inadequate response to at least a 3-month trial of a prior biologic DMARD or a targeted synthetic DMARD (e.g., Xeljanz)

iv. Intolerance to a prior biologic or targeted synthetic DMARD

v. Severely active RA that warrants a biologic DMARD as first-line therapy

2. Active polyarticular juvenile idiopathic arthritis (pJIA)
   a. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Enbrel or any other biologic DMARD indicated for active polyarticular juvenile idiopathic arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Enbrel.

   b. Authorization of 24 months may be granted for members who meet ANY of the following criteria:
      i. Member has experienced an inadequate response to at least a 3-month trial of MTX.
      ii. Member has intolerance or contraindication to MTX.
      iii. Member has experienced an inadequate response to at least a 3-month trial of a prior biologic DMARD.
      iv. Member has experienced intolerance to a prior biologic DMARD.

3. Active psoriatic arthritis (PsA)
   a. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Enbrel or any other biologic DMARD indicated for active psoriatic arthritis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Enbrel.

   b. Authorization of 24 months may be granted for members who meet ANY of the following criteria:
      i. Member has experienced an inadequate response to at least a 3-month trial of MTX, sulfasalazine, or leflunomide.
      ii. Member has intolerance or contraindication to MTX, sulfasalazine, or leflunomide.

Contraindications to MTX, sulfasalazine, or leflunomide – Examples:
- History of intolerance or adverse event
- Alcoholic liver disease or other chronic liver disease
- Elevated liver transaminases
- Interstitial pneumonitis or clinically significant pulmonary fibrosis
- Renal impairment
- Pregnancy or planning pregnancy
- Breastfeeding
- Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
- Myelodysplasia
- Hypersensitivity
- Significant drug interaction
Contraindications to MTX, sulfasalazine, or lefunomide – Examples (continued):

- Intestinal obstruction
- Urinary obstruction
- Porphyria

iii. Member has experienced an inadequate response to at least a 16-week trial of Otezla despite adequate dosing (i.e., 30 mg twice daily).

iv. Member has experienced intolerance to Otezla.

v. Member has experienced an inadequate response to at least a 3-month trial of a prior biologic DMARD.

vi. Member has experienced intolerance to a prior biologic DMARD.

vii. Member’s condition is severely active as evidenced by ANY of the following:
   a) Multiple swollen joints
   b) Structural damage in the presence of inflammation
   c) Clinically relevant extra-articular manifestations

Extra-articular manifestations of psoriatic arthritis – Examples:

- Cutaneous involvement:
  - Psoriasis
  - Erythema nodosum
  - Keratoderma blenorrhagicum
  - Circinate balanitis
  - Pyoderma gangrenosum

- Bowel involvement
  - Crohn’s disease (CD)
  - Ulcerative colitis (UC)
  - A specific colitis (in presence of inflammatory bowel disease (IBD) that cannot be classified as CD or UC)
  - Severe and persistent diarrhea

- Ocular involvement
  - Uveitis
  - Conjunctivitis

- Cardiovascular involvement
  - Aortic insufficiency
  - Conduction disturbances (e.g., atrioventricular blocks, bundle branch blocks, and intraventricular blocks)
  - Thrombosis
  - Phlebitis

- Urogenital involvement
  - Urethritis
  - Prostatitis
  - Balanitis
  - Vaginitis
  - Cervicitis amyloidosis (AA type)
  - IgA nephropathy

- Pulmonary involvement: Apical pulmonary fibrosis

viii. Member has active enthesitis and/or dactylitis (i.e., sausage digit).

ix. Member has predominant axial disease (i.e., extensive spinal involvement).
4. **Active ankylosing spondylitis (AS) and axial spondyloarthritis**
   a. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Enbrel or any other biologic DMARD indicated for active ankylosing spondylitis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Enbrel.
   
b. Authorization of 24 months may be granted for members who meet ALL of the following criteria:
      i. Member has experienced an inadequate response to at least two NSAIDs over a 4-week period in total at maximum recommended or tolerated anti-inflammatory dose, OR has intolerance and/or contraindication to 2 or more non-steroidal anti-inflammatory drugs.
      ii. Member has at least one of the following:
          a) Predominant axial disease (i.e., extensive spinal involvement)
          b) Inadequate response to a synthetic DMARD (e.g., sulfasalazine)
          c) Intolerance or contraindication to a synthetic DMARD
          d) Inadequate response to at least a 3-month trial of a prior biologic DMARD
          e) Intolerance to a prior biologic DMARD

5. **Moderate to severe chronic plaque psoriasis**
   a. Authorization of 24 months may be granted for members who have received at least a 28-day supply of Enbrel or any other biologic DMARD indicated for the treatment of moderate to severe chronic plaque psoriasis in a paid claim through a pharmacy or medical benefit within the previous 120 days of the initial request for Enbrel.
   
b. Authorization of 24 months may be granted for members who meet ALL of the following criteria:
      i. At least 5% of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
      ii. Member meets at least ONE of the following criteria:
          a) Member has experienced an inadequate response to either phototherapy (e.g., UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin despite adequate dosing and duration.
             Time to Clinical Efficacy and Dose for Pharmacologic Treatment
             - Methotrexate
               o 10 mg/week or higher for at least 1 month
             - Cyclosporine
               o 2.5 mg/kg/day or higher for at least 2 months
             - Acitretin
               o 25 mg/day or higher for at least 3 months
          b) Member has a clinical reason to avoid phototherapy or pharmacologic treatment as first-line treatment.
             Clinical Reasons to Avoid Phototherapy or Pharmacologic Treatment
             - Intolerance or adverse event to phototherapy or pharmacologic treatment
             - Phototherapy and/or pharmacologic treatment is contraindicated or cannot be used due to risk of treatment-related toxicity
             - Significant comorbidity prohibits use of systemic agents (e.g., liver or kidney disease, blood dyscrasias, uncontrolled hypertension)
             - Phototherapy is not feasible or not accessible
             - Photosensitivity or history of skin cancer
             - Concomitant use of medications that cause photosensitivity
             - Pregnancy or planning pregnancy (male or female)
             - Breastfeeding
             - Alcohol intake or alcoholic liver disease
             - Drug interaction
          c) Member has severe psoriasis that warrants a biologic DMARD as first-line therapy.
6. **Hidradenitis suppurativa**
   Authorization of 24 months may be granted for members who are prescribed Enbrel for the treatment of hidradenitis suppurativa.

7. **Reactive arthritis**
   Authorization of 24 months may be granted who are prescribed Enbrel for the treatment of reactive arthritis.

E. **CONTINUATION OF THERAPY**
   Authorization of 24 months may be granted for all members (including new members) who meet ALL initial authorization criteria and achieve or maintain positive clinical response after at least 3 months of therapy with Enbrel as evidenced by low disease activity or improvement in signs and symptoms of the condition.

F. **DOSAGE AND ADMINISTRATION**
   Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

1. **Dosing Limits**
   The following dosing limits apply:
   a. Plaque psoriasis
      • Initial loading dose for the initial 3 months: 100 mg per week; 1200 mg total for 3 months.
      • Maintenance dose: 50 mg per week
   b. All other indications
      • 50 mg per week

REFERENCES