Enbrel (etanercept)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the Enbrel drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines and clinical studies.

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

1. Moderately to severely active rheumatoid arthritis (RA)
2. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA) in patients aged 2 years or older
3. Active psoriatic arthritis (PsA)
4. Active ankylosing spondylitis (AS)
5. Chronic moderate to severe plaque psoriasis (PsO) in patients aged 4 years or older

Compendial Uses

1. Axial spondyloarthritis
2. Oligoarticular juvenile idiopathic arthritis
3. Reactive arthritis
4. Hidradenitis suppurativa, severe, refractory
5. Behcet’s disease
6. Graft versus host disease
7. Immunotherapy-related inflammatory arthritis

POLICY

Required Documentation

Submission of the following information is necessary to initiate the prior authorization review:

A) Rheumatoid arthritis (RA)
1. For initial requests:
   i. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
   ii. Laboratory results, chart notes, or medical record documentation of biomarker testing (i.e., rheumatoid factor [RF], anti-cyclic citrullinated peptide [anti-CCP], and C-reactive protein [CRP] and/or erythrocyte sedimentation rate [ESR]) (if applicable).
2. For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

B) Articular juvenile idiopathic arthritis, ankylosing spondylitis (AS), active axial spondyloarthritis, and reactive arthritis:
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response.

C) Psoriatic arthritis (PsA): For continuation requests: Chart notes or medical record documentation supporting positive clinical response.

D) Plaque psoriasis
1. Initial requests:
   i. Chart notes or medical record documentation of affected area(s) and body surface area (BSA) affected (if applicable).
   ii. Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. Continuation requests: Chart notes or medical record documentation of decreased body surface area (BSA) affected and/or improvement in signs and symptoms

E) Hidradenitis suppurativa
1. Initial requests: Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.
2. Continuation requests: Chart notes or medical record documentation supporting positive clinical response to therapy.

F) Graft versus host disease and immunotherapy-related inflammatory arthritis (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried (if applicable), including response to therapy. If therapy is not advisable, documentation of clinical reason to avoid therapy.

G) Behcet's disease (initial requests only): Chart notes, medical record documentation, or claims history supporting previous medications tried, including response to therapy (if applicable).

Criteria for Initial Approval

A. Moderately to severely active rheumatoid arthritis (RA)
1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD (e.g., Rinvoq, Xeljanz) indicated for moderately to severely active rheumatoid arthritis.

2. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
    a. Member meets either of the following criteria:
        i. Member has been tested for either of the following biomarkers and the test was positive:
            a. Rheumatoid Factor (RF)
            b. Anti-cyclic citrullinated peptide (anti-CCP)
        ii. Member has been tested for ALL of the following biomarkers:
            a. RF
            b. Anti-CCP
            c. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR)
    b. Member meets either of the following criteria:
        i. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
        ii. Member has an intolerance or contraindication to methotrexate (see Appendix A).

B. Moderately to severely active articular juvenile idiopathic arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic or targeted synthetic DMARD indicated for moderately to severely active articular juvenile idiopathic arthritis.
2. Authorization of 12 months may be granted for the treatment of moderately to severely active articular juvenile idiopathic arthritis when any of the following criteria are met:
    a. The member has had an inadequate response to methotrexate or another non-biologic DMARD administered at an adequate dose and duration.
    b. The member has risk factors (see Appendix C) and the member also meets one of the following:
        i. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
        ii. High disease activity
        iii. Are judged to be at high risk for disabling joint disease.

C. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA).

D. Active ankylosing spondylitis (AS) and active axial spondyloarthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis or active axial spondyloarthritis.
2. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis or active axial spondyloarthritis when any of the following criteria is met:
    a. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
    b. Member has an intolerance or contraindication to two or more NSAIDs.

E. Moderate to severe plaque psoriasis

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of moderate to severe plaque psoriasis.
2. Authorization of 12 months may be granted for treatment of moderate to severe plaque psoriasis in members when any of the following criteria is met:
    a. Crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
    b. At least 10% of the body surface area (BSA) is affected
    c. At least 3% of body surface area (BSA) is affected and the member meets any of the following criteria:

i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or pharmacologic treatment with methotrexate, cyclosporine or acitretin.
ii. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix B).

F. Reactive arthritis

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for reactive arthritis.
2. Authorization of 12 months may be granted for treatment of reactive arthritis when any of the following criteria is met:
   a. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to at least 15 mg/week).
   b. Member has an intolerance or contraindication to methotrexate (see Appendix A).

G. Hidradenitis suppurativa

1. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of severe, refractory hidradenitis suppurativa.
2. Authorization of 12 months may be granted for treatment of severe, refractory hidradenitis suppurativa when either of the following is met:
   a. Member has experienced an inadequate response to oral antibiotics for at least 90 days.
   b. Member has an intolerance or contraindication to oral antibiotics.

H. Graft versus host disease

Authorization of 12 months may be granted for treatment of graft versus host disease when either of the following criteria is met:

1. Member has experienced an inadequate response to systemic corticosteroids
2. Member has an intolerance or contraindication to corticosteroids.

I. Behcet's disease

1. Authorization of 12 months may be granted for members who have previously received Otezla or a biologic indicated for the treatment of Behcet's disease.
2. Authorization of 12 months may be granted for the treatment of Behcet's disease when the member has had an inadequate response to at least one nonbiologic medication for Behcet's disease (e.g., apremilast, colchicine, systemic glucocorticoids, azathioprine).

J. Immunotherapy-related inflammatory arthritis

Authorization of 12 months may be granted for treatment of severe/refractory immunotherapy-related inflammatory arthritis that is not responding to corticosteroids and anti-inflammatory agents.

Continuation of Therapy

A. Moderately to severely active rheumatoid arthritis (RA)

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active rheumatoid arthritis and who achieve or maintain a positive clinical response as evidenced by disease activity improvement of at least 20% from baseline in tender joint count, swollen joint count, pain, or disability.

B. Moderately to severely active articular juvenile idiopathic arthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderately to severely active articular juvenile idiopathic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of joints with active arthritis (e.g., swelling, pain, limitation of motion)
2. Number of joints with limitation of movement
3. Functional ability

C. Active psoriatic arthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active psoriatic arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Number of swollen joints
2. Number of tender joints
3. Dactylitis
4. Enthesitis
5. Skin and/or nail involvement

D. Active ankylosing spondylitis (AS) and active axial spondylarthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for active ankylosing spondylitis or active axial spondyloarthritis and who achieve or maintain a positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition when there is improvement in any of the following from baseline:

1. Functional status
2. Total spinal pain
3. Inflammation (e.g. morning stiffness)

E. Moderate to severe plaque psoriasis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for moderate to severe plaque psoriasis and who achieve or maintain positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

1. Reduction in body surface area (BSA) affected from baseline
2. Improvement in signs and symptoms from baseline (e.g., itching, redness, flaking, scaling, burning, cracking, pain)

F. Reactive arthritis

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for reactive arthritis and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition (e.g., tender joint count, swollen joint count, or pain).

G. Hidradenitis suppurativa

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for severe, refractory hidradenitis suppurativa and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition when any of the following is met:

1. Reduction in abscess and inflammatory nodule count from baseline
2. Reduced formation of new sinus tracts and scarring
3. Decrease in frequency of inflammatory lesions from baseline
4. Reduction in pain from baseline
5. Reduction in suppuration from baseline
6. Improvement in frequency of relapses from baseline
7. Improvement in quality of life from baseline
8. Improvement on a disease severity assessment tool from baseline

H. Graft versus host disease and immunotherapy-related inflammatory arthritis

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

I. All other diagnoses

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for an indication outlined above and who achieve or maintain positive clinical response with the requested medication as evidenced by low disease activity or improvement in signs and symptoms of the condition.

Other

For all indications: Member has had a documented negative TB test (which can include a tuberculosis skin test [PPD], an interferon release assay [IGRA], or a chest x-ray)* within 6 months of initiating therapy for persons who are naïve to biologic DMARDs or targeted synthetic DMARDs associated with an increased risk of TB.

* If the screening testing for TB is positive, there must be further testing to confirm there is no active disease. Do not administer the requested medication to members with active TB infection. If there is latent disease, TB treatment must be started before initiation of the requested medication.

For all indications: Member cannot use the requested medication concomitantly with any other biologic DMARD or targeted synthetic DMARD.

Enbrel is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosage and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. Dose optimization with 50 mg product formulations should be used when possible. Exceptions for higher quantities of 25 mg vials will be allowed when the member has a latex allergy or is following FDA-approved weight-based dosing.

Quantity Limits

Medication	Standard Limit	Exception Limit	FDA-recommended dosing
Enbrel (etanercept) 25 mg per 0.5 mL prefilled syringe	4 syringes per 28 days	None	**RA/PsA/AS** • 50 mg every week **PsO** • Loading dose: 50 mg twice a week for 3 months • Maintenance dose: 50 mg every week **Pediatric PsO/PJIA** • Weight < 63 kg: 0.8 mg per kg every week • Weight ≥ 63 kg: 50 mg every week
Enbrel (etanercept) 25 mg vial	4 vials per 28 days	8 vials per 28 days	
Enbrel (etanercept) 50 mg per 1 mL prefilled syringe/cartridge	4 syringes per 28 days	8 syringes per 28 days	
Enbrel (etanercept) 50 mg SureClick Autoinjector	4 cartridges per 28 days	8 cartridges per 28 days	

Abbreviations: RA = rheumatoid arthritis; PsA = psoriatic arthritis; AS = ankylosing spondylitis; PsO = plaque psoriasis; PJIA = polyarticular juvenile idiopathic arthritis

Appendices

Appendix A: Examples of Contraindications to Methotrexate

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease or other chronic liver disease
2. Breastfeeding
3. Blood dyscrasias (e.g., thrombocytopenia, leukopenia, significant anemia)
4. Elevated liver transaminases
5. History of intolerance or adverse event
6. Hypersensitivity
7. Interstitial pneumonitis or clinically significant pulmonary fibrosis
8. Myelodysplasia
9. Pregnancy or currently planning pregnancy
10. Renal impairment
11. Significant drug interaction

Appendix B: Examples of Clinical Reasons to Avoid Pharmacologic Treatment with Methotrexate, Cyclosporine or Acitretin.

1. Clinical diagnosis of alcohol use disorder, alcoholic liver disease, or other chronic liver disease
2. Breastfeeding
3. Drug interaction
4. Cannot be used due to risk of treatment-related toxicity
5. Pregnancy or currently planning pregnancy
6. Significant comorbidity prohibits use of systemic agents (examples include liver or kidney disease, blood dyscrasias, uncontrolled hypertension)

Appendix C: Risk Factors for articular juvenile idiopathic arthritis

1. Positive rheumatoid factor
2. Positive anti-cyclic citrullinated peptide antibodies
3. Pre-existing joint damage

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- N/A

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POLICY HISTORY

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