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Scope: Medicaid

SPECIALTY GUIDELINE MANAGEMENT

ENBREL (etanercept)

POLICY

I. 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.

A. 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. Moderate to severe chronic plaque psoriasis (PsO) in patients aged 4 years and older
6. Juvenile psoriatic arthritis in patients aged 2 years and older (JPsA)

B. 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

All other indications are considered experimental/investigational and not medically necessary.

II. 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
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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).

III. CRITERIA FOR INITIAL APPROVAL

For all indications:

- Submission of the member's chart or medical record is required, documenting medical necessity based on the criteria corresponding to the applicable indication
- Enbrel will not be used concomitantly with an injectable biologic response modifier including TNF-inhibitors (e.g., Humira (adalimumab), Remicade (infliximab), etc.) and IL-inhibitors (e.g., Cosentyx (secukinumab), Stelara (ustekinumab), Tremfya (guselkumab), Ilumya (tildrakizumab), Skyrizi (risankizumab), Bimzelx (bimekizumab), Omvoh (mirikizumab), etc.) or other oral non-biologic agent (e.g., Otezla (apremilast), Xeljanz (tofacitinib), Olumiant (baricitinib), Rinvoq (upadacitinib), Velsipity (etrasimod), etc.)

- 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.

A. **Moderately to severely active rheumatoid arthritis (RA)**
   1. Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:
      a. Enbrel is prescribed by, or in consultation with, a specialist in rheumatology.
      b. Member meets either of the following criteria:
         1. 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)
         2. 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)
      c. Member meets all of following:
         1. Member has experienced an inadequate response to at least a 3-month trial of methotrexate despite adequate dosing (i.e., titrated to 20 mg/week); OR Member has an intolerance or contraindication to methotrexate (see Appendix A)
         2. Member has had inadequate response, intolerance, or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses

B. **Moderately to severely active articular juvenile idiopathic arthritis**
   1. Authorization of 12 months may be granted for the treatment of moderately to severely active articular juvenile idiopathic arthritis when the following criteria are met: Enbrel is prescribed by, or in consultation with, a specialist in rheumatology.
   2. The member meets one of the following:
      i. The member has had an inadequate response to methotrexate or another non-biologic DMARD administered at an adequate dose and duration.

ii. The member has risk factors (See Appendix C) and the member also meets one of the following:
    1. High-risk joints are involved (e.g., cervical spine, wrist, or hip).
    2. High disease activity.
    3. Are judged to be at high risk for disabling joint disease.

3. Member has had an inadequate response, intolerance, or contraindication at maximum tolerated doses to a minimum (3) month trial of adalimumab.

C. **Active psoriatic arthritis (PsA)**

1. Authorization of 12 months may be granted for treatment of active psoriatic arthritis (PsA) in members 2 years of age and older when the following are met:
    a. Enbrel is prescribed by, or in consultation with, a specialist in dermatology or rheumatology.
    b. Member has had an inadequate response, intolerance, or contraindication at maximum tolerated doses to a minimum (3) month trial of adalimumab.

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

1. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis and axial spondyloarthritis when the following criteria is met:
    a. Enbrel is prescribed by, or in consultation with, a specialist in rheumatology.
    b. The member meets one of the following:
        i. Member has experienced an inadequate response to at least two non-steroidal anti-inflammatory drugs (NSAIDs).
        ii. Member has an intolerance or contraindication to two or more NSAIDs.
    c. Member has had an inadequate response, intolerance, or contraindication at maximum tolerated doses to a minimum (3) month trial of adalimumab.

E. **Moderate to severe chronic plaque psoriasis**

1. Authorization of 12 months may be granted for the treatment of moderate to severe chronic plaque psoriasis when all of the following are met:
    a. Enbrel is prescribed by, or in consultation with, a specialist in dermatology.
    b. At least 10 % of body surface area (BSA) is affected OR crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected.
    c. Member meets either of the following criteria:
        1. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or a pharmacologic treatment with methotrexate, cyclosporine or acitretin.
        2. Member has a clinical reason to avoid pharmacologic treatment with methotrexate, cyclosporine and acitretin (see Appendix B).
    d. Member experienced an inadequate treatment response or intolerance from Zoryve (roflumilast) cream within the last 12 months or an inadequate response, intolerance, or contraindication at maximum tolerated doses to a minimum (3) month trial of adalimumab. Contraindications, adverse effects and/or intolerance must be documented.

F. **Reactive arthritis**

1. Enbrel is prescribed by, or in consultation with, a specialist in rheumatology.
2. Authorization of 12 months may be granted for members who have previously received a biologic indicated for reactive arthritis.

3. 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 20 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 treatment of severe, refractory hidradenitis suppurativa when the following is met:
   a. Enbrel is prescribed by, or in consultation with, a specialist in dermatology.
   b. Member meets one of the following:
      i. Member has experienced an inadequate response to oral antibiotics for at least 90 days.
      ii. Member has an intolerance or contraindication to oral antibiotics.
   c. Member has had an inadequate response, intolerance, or contraindication at maximum tolerated doses to a minimum (3) month trial of adalimumab

H. **Graft versus host disease**
1. Authorization of 3 months may be granted for treatment of graft versus host disease when either of the following criteria is met:
   a. Member has experienced an inadequate response to topical or systemic corticosteroids or immunosuppressive therapy (e.g., cyclosporine or mycophenolate mofetil).
   b. Member has an intolerance or contraindication to topical or systemic corticosteroids and immunosuppressive therapy (e.g. cyclosporine, mycophenolate mofetil).

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 Behçet's disease when the member has had an inadequate response to at least one nonbiologic medication for Behçet's disease (e.g., apremilast, colchicine, systemic glucocorticoids, azathioprine).

IV. DOSING

The prescribed dose and quantity fall within the FDA-approved labeling or within compendia supported dosing guidelines.

V. 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

H. Graft versus host disease

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 in Section III 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.

VI. QUANITY LIMIT

Medication	Standard Limit	FDA-recommended dosing
Enbrel (etanercept) 25 mg per 0.5 mL prefilled syringe	8 syringes per 28 days	**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/JPsA** • Weight < 63 kg: 0.8 mg per kg every week • Weight ≥ 63 kg: 50 mg every week
Enbrel 25 mg vial	8 vials per 28 days	
Enbrel (etanercept) 50 mg per 1 mL prefilled syringe/cartridge	8 syringes per 28 days	
Enbrel 50 mg SureClick Autoinjector	8 cartridges per 28 days	

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

VII. APPENDICES

APPENDIX A: Examples of Contraindications to Methotrexate

1. Alcoholism, 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 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. Alcoholism, 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 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

VIII. REFERENCES

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