Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022, 8/2023, 2/2024, 1/2025, 08/2026 Scope: Medicaid

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) in adult patients
2. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA) in adult and pediatric patients 2 years of age or older
3. Active psoriatic arthritis (PsA) in adult patients
4. Active ankylosing spondylitis (AS) in adult patients
5. Moderate to severe plaque psoriasis (PsO) in adult and pediatric patients 4 years of age or older who are candidates for systemic therapy or phototherapy
6. Active juvenile psoriatic arthritis in pediatric patients 2 years of age or 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. 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; AND
- Physician has assessed baseline disease severity utilizing an objective measure/tool; AND
- Enbrel will not be used concomitantly with an injectable biologic response modifier including TNF-inhibitors (e.g., adalimumab (e.g., Hadlima), Enbrel (etanercept), Remicade (infliximab), Simponi (golimumab), etc.) and IL-inhibitors (e.g., Cosentyx (secukinumab), ustekinumab

(e.g., Stelara, Otulfi, Selarsdi, Steqeyma, and Yesintek, etc.), Tremfya (guselkumab), Icotyde (icotrokinra), Ilumya (tildrakizumab), Skyrizi (risankizumab), Omvoh (mirikizumab), etc.) or other oral non-biologic agent (e.g., Otezla (apremilast), tofacitinib (Xeljanz), Olumiant (baricitinib), Rinvoq (upadacitinib), etc.); AND

- Member is free of any clinically important active infection, including clinically important localized infections; AND
- Member will not receive live vaccines during therapy; AND
- Member has been evaluated and screened for the presence of latent tuberculosis (TB) infection prior to initiating treatment and will receive ongoing monitoring for the presence of TB during treatment.

A. Moderately to severely active rheumatoid arthritis (RA)

Authorization of 12 months may be granted for treatment of moderately to severely active RA when all of the following criteria are met:

1. Member is 18 years of age or older; AND
2. Prescribed by, or in consultation with, a specialist in rheumatology; AND
3. Documentation has been submitted of one of the following criteria:
    a. Member has been tested for either of the following biomarkers and the test was positive:
        i. Rheumatoid factor (RF)
        ii. Anti-cyclic citrullinated peptide (anti-CCP); OR
    b. Member has been tested for ALL of the following biomarkers:
        i. RF
        ii. Anti-CCP
        iii. C-reactive protein (CRP) and/or erythrocyte sedimentation rate (ESR); AND
4. Documentation has been submitted that the member meets both of the following criteria:
    a. Member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of methotrexate (see Appendix A) or any other conventional disease-modifying antirheumatic drug (DMARD) at maximum tolerated doses; AND
    b. Member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses.

B. Moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA)

Authorization of 12 months may be granted for the treatment of moderately to severely active articular juvenile idiopathic arthritis when all of the following criteria are met:

1. Member is 2 years of age or older; AND
2. Prescribed by, or in consultation with, a specialist in rheumatology; AND
3. Documentation has been submitted of one of the following criteria:
    a. Member has had an inadequate response, intolerance, or contraindication to at least a 1-month trial of either an oral non-steroidal anti-inflammatory drug (NSAID) OR if the member is 18 years of age or older, an oral disease-modifying anti-rheumatic

agent (DMARD) (e.g., methotrexate, leflunomide, sulfasalazine, etc.) at an adequate dose or duration; OR

b. Member has risk factors for disease severity and potentially a more refractory disease course (see Appendix E), and also meets one of the following:
    i. High-risk joints are involved (e.g., cervical spine, wrist, or hip)
    ii. High disease activity
    iii. Is judged to be at high risk for disabling joint disease; AND

4. Documentation has been submitted that the member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses.

C. Active psoriatic arthritis (PsA)

Authorization of 12 months may be granted for treatment of active psoriatic arthritis when all of the following criteria are met:

1. Member is 2 years of age or older; AND
2. Prescribed by, or in consultation with, a specialist in dermatology or rheumatology; AND
3. Documentation has been submitted indicating one of the following criteria:
    a. Member has mild to moderate disease and meets one of the following criteria:
        i. Member has had an inadequate response, intolerance, or contraindication to methotrexate or another conventional disease-modifying anti-rheumatic agent (DMARD) (e.g., leflunomide, sulfasalazine, etc.) despite adequate dosing; OR
        ii. Member has enthesitis or predominantly axial disease; OR
    b. Member has severe disease; AND
4. If member is 18 years of age or older, documentation has been submitted that the member has experienced an inadequate response, intolerance or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses AND a 6-month trial of ustekinumab biosimilar at maximum tolerated doses.
5. If member is 6 years of age or older but under 18, documentation has been submitted that the member has experienced an inadequate response, intolerance or contraindication to at least a 6-month trial of ustekinumab biosimilar at maximum tolerated dose

D. Active ankylosing spondylitis (AS)

Authorization of 12 months may be granted for treatment of active ankylosing spondylitis when all of the following criteria are met:

1. Member is 18 years of age or older; AND
2. Prescribed by, or in consultation with, a specialist in rheumatology; AND
3. Documentation has been submitted of all of the following:
    a. Member has had an inadequate response, intolerance or contraindication to at least two (2) NSAIDs; AND
    b. Member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses.

E. Moderate-to-severe plaque psoriasis (PsO)

Authorization of 12 months may be granted for the treatment of moderate to severe plaque psoriasis when all of the following criteria are met:

1. Member is 12 years of age or older; AND
2. Prescribed by, or in consultation with, a dermatologist; AND
3. Documentation has been submitted of one or more of the following:
   a. BSA affected is at least 10%; OR
   b. Crucial body areas affected (e.g., face, hands, feet, genitals, scalp); OR
   c. Inadequate treatment response to topical therapy (corticosteroids, calcineurin inhibitors (e.g., tacrolimus), vitamin D analogs (e.g., calcipotriene), retinoids (e.g., tazarotene)); AND
4. Documentation has been submitted that the member meets any of the following criteria:
   a. Member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of a conventional oral agent for PsO (e.g., methotrexate, cyclosporine, or acitretin); OR
   b. Member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of phototherapy (e.g., UVB, PUVA); OR
   c. Clinical rationale has been provided indicating member's disease severity warrants a biologic DMARD as first-line therapy; AND
5. Documentation has been submitted that the member meets either of the following criteria:
   a. If member is 18 years of age or older, member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of adalimumab AND a 6-month trial of ustekinumab biosimilar; OR
   b. If member is 6 years of age or older but under 18, member has had an inadequate response, intolerance, or contraindication to at least a 6-month trial of ustekinumab biosimilar.

F. **Reactive arthritis**

Authorization of 12 months may be granted for treatment of reactive arthritis when all of the following criteria are met:

1. Prescribed by, or in consultation with, a specialist in rheumatology; AND
2. Documentation has been submitted that the member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of methotrexate despite adequate dosing.

G. **Hidradenitis suppurativa**

Authorization of 12 months may be granted for treatment of severe, refractory hidradenitis suppurativa when all of the following criteria are met:

1. Prescribed by, or in consultation with, a specialist in dermatology or rheumatology; AND
2. Documentation has been submitted that the member meets both of the following criteria:

a. Member has had an inadequate response, intolerance, or contraindication to oral antibiotics for at least 90 days; AND
b. Member has had an inadequate response, intolerance, or contraindication to at least a 3-month trial of adalimumab at maximum tolerated doses.

H. **Graft versus host disease**
Authorization of 12 months may be granted for treatment of graft versus host disease when all of the following criteria are met:
1. Prescribed by, or in consultation with, a specialist in oncology or hematology; AND
2. Documentation has been submitted that the member has had an inadequate response, intolerance, or contraindication to topical or systemic corticosteroids OR immunosuppressive therapy (e.g., cyclosporine or mycophenolate mofetil).

I. **Behcet's disease**
Authorization of 12 months may be granted for treatment of Behcet's disease when all of the following criteria are met:
1. Prescribed by, or in consultation with, a specialist in rheumatology; AND
2. Documentation has been submitted that the member has had an inadequate response, intolerance, or contraindication to at least one nonbiologic medication for Behcet's disease (e.g., azathioprine, colchicine, cyclosporine, systemic corticosteroids).

III. CONTINUATION OF THERAPY

A. Moderately to severely active rheumatoid arthritis (RA)
Authorization of 12 months may be granted for all adult members (including new members) with documentation of 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 (JIA)
Authorization of 12 months may be granted for all members 2 years of age or older (including new members) with documentation of 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 (PsA)

Authorization of 12 months may be granted for all members 2 years of age or older (including new members) with documentation of 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. Axial disease
6. Skin and/or nail involvement
7. Functional status
8. C-reactive protein (CRP)

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

Authorization of 12 months may be granted for all adult members (including new members) with documentation of 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)
4. Swollen joints
5. Tender joints
6. C-reactive protein (CRP)

E. Moderate to severe plaque psoriasis

Authorization of 12 months may be granted for all members 4 years of age or older (including new members) with documentation 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 (e.g., reduction in BSA from baseline) or improvement in signs and symptoms of the condition (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) with documentation of 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) with documentation of 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

Authorization of 12 months may be granted for all members (including new members) who are using the requested medication for chronic graft versus host disease and who achieve or maintain a positive clinical response as evidenced by low disease activity or improvement in signs and symptoms of the condition.

I. Behcet's disease

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

IV. 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**
Enbrel 25 mg vial	8 vials per 28 days	
Enbrel (etanercept) 50 mg per 1 mL prefilled syringe/cartridge	8 syringes per 28 days	

Medication	Standard Limit	FDA-recommended dosing
Enbrel 50 mg SureClick Autoinjector	8 cartridges per 28 days	• Weight < 63 kg: 0.8 mg per kg every week • Weight ≥ 63 kg: 50 mg every week

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

V. 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

VI. REFERENCES

1. Enbrel [package insert]. Thousand Oaks, CA: Immunex Corporation; January 2026. Accessed April 2026.
2. van der Heijde D, Ramiro S, Landewe R, et al. 2016 Update of the international ASAS-EULAR management recommendations for axial spondyloarthritis. *Ann Rheum Dis.* 2017;0:1-14.
3. Flagg SD, Meador R, Hsia E, et al. Decreased pain and synovial inflammation after etanercept therapy in patients with reactive and undifferentiated arthritis: an open-label trial. Arthritis Rheum. 2005;53(4):613-617.
4. DRUGDEX® System [Internet database]. Ann Arbor, MI: Truven Health Analytics. Updated periodically. Accessed August 17, 2019.
5. Smolen JS, Landewé R, Billsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. *Ann Rheum Dis.* 2017*;0*:1-18.
6. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. *Arthritis Rheumatol.* 2016;68(1)1-26.
7. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Rheum*. 2008;59(6):762-784.
8. Beukelman T, Patkar NM, Saag KG, et al. 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis: initiation and safety monitoring of therapeutic agents for the treatment of arthritis and systemic features. *Arthritis Care Res.* 2011;63(4):465-482.
9. Menter A, Gottlieb A, Feldman SR, et al. Guidelines for the management of psoriasis and psoriatic arthritis. Section 1: Overview of psoriasis and guidelines of care for the treatment of psoriasis with biologics. *J Am Acad Dermatol.* 2008;58(5):826-850.
10. Menter A, Korman NJ, Elmets CA, et al. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 6: Guidelines of care for the treatment of psoriasis and psoriatic arthritis: case-based presentations and evidence-based conclusions. *J Am Acad Dermatol.* 2011;65(1):137-174.
11. Gossec L, Smolen JS, Ramiro S, et al. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies; 2015 update. *Ann Rheum Dis*. 2016;75(3):499-510.
12. Gladman DD, Antoni C, P Mease, et al. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis.* 2005;64(Suppl II):ii14–ii17.
13. Peluso R, Lervolino S, Vitiello M, et al. Extra-articular manifestations in psoriatic arthritis patients. [Published online ahead of print May 8, 2014]. *Clin Rheumatol.* 2014.Accessed August 22, 2014.
14. Braun J, van den Berg R, Baraliakos X, et al. 2010 update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Ann Rheum Dis* 2011;70:896–904.
15. Ward MM, Deodhar A, Akl EA, et al. American College of Rheumatology/Spondylitis Association of America/Spondyloarthritis Research and Treatment Network 2015 recommendations for

the treatment of ankylosing spondylitis and nonradiographic axial spondyloarthritis. *Arthritis Rheumatol.* 2015: 10.1002/art.39298. [Epub ahead of print].

16. Martin PJ, Rizzo JD, Wingard JR, et al. First and second line systemic treatment of acute graft versus host disease: Recommendations of the American Society of Blood and Marrow Transplantation. Biol Blood Marrow Transplant 18:1150-1163, 2012.
17. Hatemi G, Christensen R, Bodaghi, et al. 2018 update of the EULAR recommendations for the management of Behcet's syndrome. Ann Rheum Dis. 2018.; 77: 808-818.
18. Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. J Am Acad Dermatol. 2019;80(4):1029-1072.
19. Tuberculosis (TB). TB risk factors. Centers for Disease Control and Prevention. Retrieved on 21 June 2019 from: https://www.cdc.gov/tb/topic/basics/risk.htm.