

Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022
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

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.

Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022
Scope: Medicaid

- 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).

III. CRITERIA FOR INITIAL APPROVAL

For all indications:

- Prior Authorization Request is submitted by the Provider's office; AND
- Prior Authorization Request is not submitted by a pharmacy or another third party; AND
- Submission of the member's chart or medical record is required, documenting medical necessity based on the criteria corresponding to the applicable indication
- 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

Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022
Scope: Medicaid

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 either 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).
 2. Member has an intolerance or contraindication to methotrexate (see Appendix A)

B. Moderately to severely active articular juvenile idiopathic 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 moderately to severely active articular juvenile idiopathic arthritis.
3. 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) and Enbrel is prescribed by, or in consultation with, a specialist in dermatology or rheumatology.

D. Active ankylosing spondylitis (AS) and axial spondyloarthritis

Enbrel is prescribed by, or in consultation with, a specialist in rheumatology.

Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022
Scope: Medicaid

- 1.
2. Authorization of 12 months may be granted for members who have previously received a biologic indicated for active ankylosing spondylitis or axial spondyloarthritis.
3. Authorization of 12 months may be granted for treatment of active ankylosing spondylitis and 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 chronic plaque psoriasis

1. Enbrel is prescribed by, or in consultation with, a specialist in dermatology.
2. 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 chronic plaque psoriasis.
3. Authorization of 12 months may be granted for treatment of moderate to severe chronic plaque psoriasis when all of the following criteria are met:
 - a. 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.
 - b. Member meets any of the following criteria:
 - i. Member has had an inadequate response or intolerance to either phototherapy (e.g., UVB, PUVA) or a 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).
 - iii. Member experienced an inadequate treatment response or intolerance from Zoryve (roflumilast) cream within the last 12 months. Contraindications, adverse effects and/or intolerance must be documented.
 1. If the member is switching from a biologic for psoriasis treatment, they are not required to trial Zoryve before Enbrel
 - iv. Member has severe psoriasis that warrants a biologic DMARD as first-line therapy (i.e. at least 10% of the body surface area (BSA) or crucial body areas (e.g., hands, feet, face, neck, scalp, genitals/groin, intertriginous areas) are affected).

1. **Reactive arthritis** 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).

F. Hidradenitis suppurativa

1. Enbrel is prescribed by, or in consultation with, a specialist in dermatology.
2. Authorization of 12 months may be granted for members who have previously received a biologic indicated for the treatment of severe, refractory hidradenitis suppurativa.

Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022
Scope: Medicaid

3. 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.

G. 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 topical or systemic corticosteroids or immunosuppressive therapy (e.g., cyclosporine or mycophenolate mofetil).
2. 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 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).

IV. DOSING

- a. 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

Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022
Scope: Medicaid

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

Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022
Scope: Medicaid

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. QUANTITY 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 <ul style="list-style-type: none"> 50 mg every week PsO <ul style="list-style-type: none"> Loading dose: 50 mg twice a week for 3 months Maintenance dose: 50 mg every week Pediatric PsO/PJIA <ul style="list-style-type: none"> 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

Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022
Scope: Medicaid

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

1. Enbrel [package insert]. Thousand Oaks, CA: Immunex Corporation; April 2021.
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.

Effective date: 7/15/2020
Review date: 5/2020, 9/2020, 12/2020, 5/2021, 6/2022, 12/2022
Scope: Medicaid

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>.