

## Clinical Policy: Etanercept (Enbrel)

Reference Number: AZ.CP.PHAR.18

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Line of Business: Arizona Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

Etanercept (Enbrel<sup>®</sup>) is a Tumor Necrosis Factor Inhibitor (TNFi).

### FDA approved indications:

Enbrel is indicated for:

- **Rheumatoid Arthritis:** Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage and improving physical function in adult patients with moderately to severely active rheumatoid arthritis (RA). Enbrel can be initiated in combination with methotrexate (MTX) or used alone.
- **Moderately to Severely Active Polyarticular Juvenile Idiopathic Arthritis:** Reducing signs and symptoms of moderately to severely active Polyarticular juvenile arthritis (PJIA) in patients ages 2 and older.
- **Psoriatic Arthritis (PsA):** Reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function. Enbrel can be used with or without methotrexate.
- **Chronic moderate to severe plaque psoriasis:** Treatment of patients 4 years or older with chronic moderate to severe plaque psoriasis (PP) who are candidates for systemic therapy or phototherapy.
- **Ankylosing Spondylitis:** Reducing signs and symptoms in patients with active ankylosing spondylitis (AS).

### Policy/Criteria

*Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria*

It is the policy of health plans affiliated with Centene Corporation<sup>®</sup> that Enbrel is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria

##### A. Rheumatoid Arthritis (must meet all):

1. Diagnosis of RA;
2. One of the following (a or b):
  - a. Prescribed by or in consultation with a rheumatologist;
  - b. Defined at baseline prior to disease modifying anti-rheumatic drug (DMARD) treatment initiation by the (American College of Rheumatology (ACR)) criteria (refer to General Information for ACR criteria)

3. One of the following (a or b):
  - a. Failure of a trial of MTX, at a dose of at least 15mg per week, in the last year for patients who are new to biologics unless contraindicated or clinically significant adverse effects are experienced;
  - b. If patient is not a candidate for MTX (i.e., patient is a smoker (increased risk of MTX lung disease) or if MTX is otherwise contraindicated), then failure of a trial of sulfasalazine or one other DMARD;
4. Dose does not exceed 50 mg once weekly.

**Approval duration 3 months**

#### **B. Psoriatic Arthritis**

1. Diagnosis of active PsA at baseline prior to DMARD therapy;
2. Prescribed by or in consultation with a rheumatologist or dermatologist;
3. Failure of a trial of MTX, at a dose of at least 15 mg per week, in the last year for patients who are new to biologics unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 50 mg weekly.

**Approval duration: 3 months**

#### **C. Polyarticular Juvenile Idiopathic Arthritis**

1. Diagnosis of active PJIA;
2. Prescribed by or in consultation with a rheumatologist;
3. Failure of a trial of MTX for three months unless contraindicated or clinically significant adverse effects are experienced;
4. Dose does not exceed 50 mg weekly.

**Approval duration: 3 months**

#### **D. Plaque Psoriasis**

1. Diagnosis of moderate to severe PP;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. One of the following (a, b, or c):
  - a. Psoriasis affects 5% or more of the body;
  - b. Psoriasis involves hands, feet, head and neck or genitalia;
  - c. Failure of topical therapy (e.g., calcipotriene, Tazorac<sup>®</sup>, topical steroids);
4. Failure of a trial of ONE of the following therapies (a or b), either alone or in combination, unless contraindicated or clinically significant adverse effects are experienced:
  - a. MTX up to a dose of 15-20 mg/week;
  - b. If MTX is contraindicated, failure or clinically significant adverse effects to PUVA / UVB therapy or cyclosporine;
5. Dose does not exceed 50 mg twice weekly.

**Approval duration: 3 months**

#### **E. Ankylosing Spondylitis**

1. Diagnosis of moderate to severe AS;

2. Failure of at least two NSAIDs for at least 3 months at maximal recommended or tolerated anti-inflammatory doses, unless contraindicated or clinically significant adverse effects are experienced
3. Dose does not exceed 50 mg weekly.

**Approval duration: 3 months**

**F. Other diagnoses/indications**

1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

**II. Continued Therapy**

**A. All Indications in Section I (must meet all):**

1. Currently receiving medication via a health plan affiliated with Centene Corporation or member has previously met initial approval criteria;
2. Documentation of positive response to therapy;
3. If request is for a dose increase, new dose does not exceed dose listed in section I for the relevant indication.

**Approval duration: Up to one year**

**B. Other diagnoses/indications (must meet 1 or 2):**

1. Currently receiving medication via a health plan affiliated with Centene Corporation and documentation supports positive response to therapy.

**Approval duration: Duration of request or 12 months (whichever is less); or**

2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized)

**III. Diagnoses/Indications for which coverage is NOT authorized:**

- A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – CP.PHAR.57 or evidence of coverage documents;
- B.** Combination use with Xeljanz or biologic DMARDs such as tumor necrosis factor antagonists (Cimzia, Humira, Simponi, Remicade), interleukin-1 receptor (IL-1R) antagonists (Kineret), interleukin-6 receptor (IL6R) antagonists (Actemra), anti-CD20 monoclonal antibodies (Rituxan) and selective co-stimulation modulators (Orencia) because of the possibility of increased immunosuppression, neutropenia and increased risk of infection.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

DMARD: disease modifying anti-rheumatic drug

NSAID: non-steroidal anti-inflammatory drug

RA: rheumatoid arthritis

PJIA: Polyarticular juvenile arthritis

PsA: Psoriatic Arthritis

PP: plaque psoriasis

AS: ankylosing spondylitis

MTX: methotrexate

*Appendix B: General Information*

- ACR Classification criteria for RA (score-based algorithm: add score of categories A-D; a score of  $\geq 6/10$  is needed for classification of a patient as having definite RA).
  - A. Joint involvement (swollen or tender)
    - 1 large joint, score = 0
    - 2-10 large joints, score = 1
    - 1-3 small joints (with or without involvement of large joints), score = 2
    - 4-10 small joints (with or without involvement of large joints), score = 3
    - $>10$  joints (at least 1 small joint), score = 5
  - B. Serology (at least 1 test result is needed for classification)
    - Negative RF (rheumatoid factor) and negative ACPA (anti-citrullinated protein antibody), score = 0
    - Low-positive RF or low-positive ACPA, score = 2
    - High-positive RF or high-positive ACPA, score = 3
  - C. Acute-phase reactants (at least 1 test result is needed for classification)
    - Normal CRP (C-reactive protein) and normal ESR (erythrocyte sedimentation rate), score = 0
    - Abnormal CRP or abnormal ESR, score = 1
  - D. Duration of symptoms
    - $< 6$  weeks, score = 0
    - $\geq 6$  weeks, score = 1
- In RA, failure of MTX or DMARD is defined as a contraindication or  $\leq 50\%$  decrease in swollen joint count,  $\leq 50\%$  decrease in tender joint count, and  $\leq 50\%$  decrease in ESR, or  $\leq 50\%$  decrease in CRP, or contraindication to at least 3 months of therapy with MTX at doses up to 25 mg per week or maximum tolerated dose.
- This agent is immunosuppressive and has the potential to increase the risk of infection and reactivate latent, chronic infections. It should not be administered to patients with a clinically important infection. Caution should be used in patients with chronic infections or history of recurrent infection. If patient develops a serious infection this agent should be discontinued.
- Two clinical trials of two years duration failed to demonstrate that TNF inhibition reduced radiographic progression of structural damage.
- Several ankylosing spondylitis (AS) treatment guidelines call for a trial of 2 or 3 non-steroidal anti-inflammatory drugs (NSAID) prior to use of an anti-TNF agent. A two year trial showed that continuous NSAID use reduced radiographic progression of AS versus on demand use of NSAID.
- Serious infections were seen in clinical studies with concurrent use of Kineret and another TNF-blocking agent, with no added benefit compared to Enbrel alone. Because of the nature of the adverse reactions with this combination therapy, similar toxicities may also result from combination of anakinra and other tumor necrosis factor (TNF) blocking agents.
- Failure of MTX in PJIA is defined as disease activity remaining moderate to high despite treatment with MTX.
- In PJIA, response to treatment is reflected by improvement of disease activity level and poor prognostic features including: reduction in the number of active joints, ESR

- or CRP, Physician global assessment, patient/parent global assessment, arthritis of the hip or cervical spine, positive RF or ACPA, radiographic damage.
- Per prescribing information, Xeljanz should not be used in combination with biologic DMARDs.
- Enbrel has a Class IIa recommendation for use for severe, refractory hidradenitis suppurative per MicroMedex.

*Appendix C: Therapeutic Alternatives*

<b>Drug</b>	<b>Dosing Regimen</b>	<b>Dose/Limit/Maximum Dose</b>
Imuran (azathioprine)	<b>Rheumatoid Arthritis</b> 1 mg/kg/day (50-100 mg) PO given as a single dose or in divided doses twice daily	2.5 mg/kg/day
Dovonex <sup>®</sup> (calcipotriene)	<b>Plaque Psoriasis</b> Apply topically QD or BID	100 g/wk (adults) 50 g/wk (adolescents)
Cimzia <sup>®</sup> (certolizumab pegol)**	<b>Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis</b> 400 mg SC initially and at Weeks 2 and 4. Maintenance dose: 200 mg SC every other week or 400 mg SC every 4 weeks	Initial: 1200 mg Maintenance: 400 mg/month
Gengraf, Neoral (Cyclosporine)	<b>Rheumatoid Arthritis, Plaque Psoriasis</b> 2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day
Humira (adalimumab)*	<b>Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis</b> 40 mg QOW <b>Plaque Psoriasis</b> 80 mg one time, followed by 40 mg QOW	40 mg weekly
Plaquenil <sup>®</sup> (hydroxychloroquine)	<b>Rheumatoid Arthritis</b> Initial dose: 400-600 mg PO daily Maintenance dose: 200-400 mg PO daily	600 mg/day

\*Require prior authorization

\*\*Non-Formulary

Therapeutic alternatives are listed as Brand name<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) when the drug is available by both brand and generic.

**V. Dosage and Administration**

<b>Indication</b>	<b>Dosing Regimen</b>	<b>Maximum Dose</b>
Rheumatoid Arthritis; Psoriatic Arthritis; Ankylosing spondylitis	50 mg SC once weekly (May be given as 25mg BIW)	50 mg weekly

Polyarticular Juvenile Idiopathic Arthritis	Less than 63 kg: 0.8 mg/kg SC per week given as single injection. Maximum dose of 50 mg per week 63 kg or more: 50 mg SC per week (50 mg dose may be given once weekly or as 25 mg BIW)	50 mg weekly
Plaque Psoriasis	Starting dose: 50 mg or 25 mg SC twice weekly for 3 months Maintenance dose: 50 mg or 25mg SC once weekly (50 mg dose may be given once weekly or as 25 mg BIW)	50 mg weekly

## VI. Product Availability

Drug	Availability
Etanercept (Enbrel)	Solution for injection: 25 mg vial
Etanercept (Enbrel)	Solution for injection: 25 and 50 mg prefilled syringe
Etanercept (Enbrel) SureClick	Solution for injection: 50mg prefilled autoinjector
Etanercept (Enbrel) Mini	Solution for injection: 50 mg/mL cartridge solution

## VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template; minor changes to verbiage and grammar. References updated.	07.07.17	11.17
Added Enbrel Mini to product availability and changed dosing info for alternative agents. References updated.	9.12.18	

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note: For Medicaid members,** when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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