Clinical Policy: Etanercept (Enbrel)

Reference Number: IN.PHAR.250
Effective Date: 08.16
Last Review Date: 08.21
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Etanercept (Enbrel®) is a tumor necrosis factor (TNF) blocker.

FDA Approved Indication(s)

Enbrel is indicated for the treatment of:

- For reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in patients with moderately to severely active rheumatoid arthritis (RA). Enbrel can be initiated in combination with methotrexate (MTX) or used alone.
- For reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) in patients ages 2 and older
- For reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis (PsA). Enbrel can be used with or without methotrexate.
- For reducing signs and symptoms in patients with active ankylosing spondylitis (AS)
- For the treatment of patients 4 years or older with chronic moderate to severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

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

I. Initial Approval Criteria

A. Ankylosing Spondylitis (must meet all)**:**

1. Diagnosis of AS;
2. Dose does not exceed 50 mg every week.

Approval duration: 12 months

B. Plaque Psoriasis (must meet all)**:**

1. Diagnosis of moderate-to-severe PsO
2. Meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses;

b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;

3. Dose does not exceed one of the following (a or b):
   a. Adults: 50 mg twice weekly for 3 months, followed by maintenance dose of 50 mg every week;
   b. Pediatrics (*see Appendix E for dose rounding guidelines*) (i or ii):
      i. Weight < 63 kg: 0.8 mg/kg every week;
      ii. Weight ≥ 63 kg: 50 mg every week.

Approval duration: 12 months

C. Polyarticular Juvenile Idiopathic Arthritis:

1. Diagnosis of Polyarticular Juvenile Idiopatic Arthrit
2. Dose does not exceed one of the following (a or b):
   a. Adults: 50 mg every week;
   b. Pediatrics (*see Appendix E for dose rounding guidelines*) (i or ii):
      i. Weight < 63 kg: 0.8 mg/kg every week;
      . Weight ≥ 63 kg: 50 mg every week.

Approval duration: 12 months

D. Psoriatic Arthritis (must meet all)**:**

1. Diagnosis of Psoriatic Arthritis
2. Dose does not exceed 50 mg every week.

Approval duration: 12 months

E. Rheumatoid Arthritis (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of at least ONE conventional disease-modifying anti-rheumatic drug [DMARD] (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
2. Dose does not exceed 50 mg every week.

Approval duration: 12 months

F. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Member has 90 days of utilization history.

2. If request is for a dose increase, new dose does not exceed 50 mg every week. **Approval duration: 12 months**

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.PMN.53 for Medicaid.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
AS: ankylosing spondylitis
CDAI: clinical disease activity index
cJADAS: clinical juvenile arthritis disease activity score
DMARD: disease-modifying anti rheumatic drug
FDA: Food and Drug Administration
GI: gastrointestinal
MTX: methotrexate
NSAID: non-steroidal anti-inflammatory drug
PsO: plaque psoriasis
PJIA: polyarticular juvenile idiopathic arthritis
PsA: psoriatic arthritis
RA: rheumatoid arthritis
RAPDI3: routine assessment of patient index data 3
TNF: tumor necrosis factor

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin (Soriatane®)	**PsO** 25 or 50 mg PO QD	50 mg/day
azathioprine (Azasan®, Imuran®)	**RA** 1 mg/kg/day PO QD or divided BID	2.5 mg/kg/day
Cuprimine□ (d-penicillamine)	**RA*** Initial dose: 125 or 250 mg PO QD Maintenance dose: 500 – 750 mg/day PO QD	1,500 mg/day
cyclosporine (Sandimmune®, Neoral®)	**PsO** 2.5 mg/kg/day PO divided BID **RA** 2.5 – 4 mg/kg/day PO divided BID	4 mg/kg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
hydroxychloroquine (Plaquenil®)	**RA*** Initial dose: 400 – 600 mg/day PO QD Maintenance dose: 200 – 400 mg/day PO QD	600 mg/day
leflunomide (Arava®)	**PJIA*** Weight < 20 kg: 10 mg every other day Weight 20 - 40 kg: 10 mg/day Weight > 40 kg: 20 mg/day **RA** 100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
methotrexate (Rheumatrex®)	**PsO** 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week **PJIA*** 10 – 20 mg/m²/week PO, SC, or IM **RA** 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week	30 mg/week
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS** Varies	Varies
Ridaura® (auranofin)	**RA** 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine®)	**PJIA*** 30-50 mg/kg/day PO divided BID **RA** 2 g/day PO in divided doses	PJIA: 2 g/day RA: 3 g/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): patients with sepsis
- Boxed warning(s):
  - Serious infections
  - Malignancies

Appendix D: General Information

- Definition of failure of MTX or DMARDs
    - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
    - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.
- Examples of positive response to therapy may include, but are not limited to:
    - Reduction in joint pain/swelling/tenderness
    - Improvement in ESR/CRP levels
    - Improvements in activities of daily living
- Hidradenitis suppurativa:
    - HS is sometimes referred to as: "acne inversa, acne conglobata, apocrine acne, apocrinitis, Fox-den disease, hidradenitis axillaris, HS, pyodermia sinifica fistulans, Velpeau's disease, and Verneuil's disease."
    - Per the 2019 North American guidelines for HS, the limited available evidence does not support use of etanercept for HS. One randomized, double-blind, placebo-controlled study (n = 20) demonstrated no statistically significant improvement in patient or physician-reported outcomes. Other studies demonstrated either mixed evidence or the limited efficacy was determined using incompletely validated outcome measures.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RA	25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week
PsA		
AS	50 mg SC once weekly	50 mg/week
PJIA	Weight < 63 kg: 0.8 mg/kg SC once weekly Weight ≥ 63 kg: 50 mg SC once weekly	50 mg/week
PsO	*Adults:* Initial dose:	50 mg/week
	50 mg SC twice weekly for 3 months Maintenance dose:	
	50 mg SC once weekly *Pediatrics:* Weight < 63 kg: 0.8 mg/kg SC once weekly Weight ≥ 63 kg: 50 mg SC once weekly	

V. Product Availability

- Single-dose prefilled syringe: 25 mg/0.5 mL, 50 mg/mL

- Single-dose prefilled SureClick® autoinjector: 50 mg/ml
- Single-dose vial: 25 mg/0.5 mL
- Multi-dose vial for reconstitution: 25 mg
- Enbrel Mini™ single-dose prefilled cartridge for use with AutoTouch™ reusable autoinjector: 50 mg/mL

VI. References

1. Enbrel Prescribing Information. Thousand Oaks, CA: Immunex Corporation: August 2020. Available at https://www.enbrel.com/. Accessed January 20, 2021.
2. 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.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J1438	Injection, etanercept, 25 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Created for IN Medicaid PA Alignment	08.21	OMPP approved

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.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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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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