

Clinical Policy: Etanercept (Enbrel)

Reference Number: CP.PHAR.250

Effective Date: 08.16

Last Review Date: 11.18

Line of Business: HIM, 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 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. Rheumatoid Arthritis (must meet all):

1. Diagnosis of RA;
2. Prescribed by or in consultation with a rheumatologist;
3. Age \geq 18 years;
4. Member meets one of the following (a or b):
 - a. Failure of a \geq 3 consecutive month trial of methotrexate (MTX) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
 - b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a \geq 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;

5. Dose does not exceed 50 mg every week.

Approval duration: 6 months

B. Polyarticular Juvenile Idiopathic Arthritis (must meet all):

1. Diagnosis of PJIA;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 2 years;
4. Member meets one of the following (a or b):
 - a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
 - b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of sulfasalazine or leflunomide at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed one of the following (a or b):
 - a. Adults: 50 mg every week;
 - b. Pediatrics (i or ii):
 - i. Weight < 63 kg: 0.8 mg/kg every week;
 - ii. Weight ≥ 63 kg: 50 mg every week.

Approval duration: 6 months

C. Psoriatic Arthritis (must meet all):

1. Diagnosis of PsA;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a, b, or c), unless contraindicated or clinically significant adverse effects are experienced:
 - a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses;
 - b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of cyclosporine, sulfasalazine, or leflunomide at up to maximally indicated doses;
 - c. For axial disease, failure of a ≥ 4 week-trial of non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses;
5. Dose does not exceed 50 mg every week.

Approval duration: 6 months

D. Ankylosing Spondylitis (must meet all):

1. Diagnosis of AS;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;

4. Failure of at least TWO non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses, each used for ≥ 4 weeks unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 50 mg every week.

Approval duration: 6 months

E. Plaque Psoriasis (must meet all):

1. Diagnosis of PsO;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 4 years;
4. Member meets one of the following (a or b):
 - a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
 - b. If intolerance or contraindication to MTX (*see Appendix D*), failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
5. 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 (i or ii):
 - i. Weight < 63 kg: 0.8 mg/kg every week;
 - ii. Weight ≥ 63 kg: 50 mg every week.

Approval duration: 6 months

F. Hidradenitis Suppurativa (off-label) (must meet all):

1. Diagnosis of HS;
2. Prescribed by a dermatologist, rheumatologist, or gastrointestinal (GI) specialist;
3. Age ≥ 18 years;
4. Documentation of Hurley stage II or stage III (*see Appendix D*);
5. Failure of a ≥ 3 consecutive month trial of systemic antibiotic therapy (e.g., clindamycin, minocycline, doxycycline, rifampin) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
6. Failure of a ≥ 3 consecutive month trial of adalimumab (*Humira[®] is preferred*) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
**Prior authorization is required for adalimumab*
7. Request meets one of the following (a or b):
 - a. 50 mg twice weekly;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

G. 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): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
 - a. For HS, i or ii:
 - i. 50 mg twice weekly;
 - ii. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
 - b. For all other indications: 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): HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AS: ankylosing spondylitis

DMARD: disease-modifying anti
rheumatic drug

FDA: Food and Drug Administration

GI: gastrointestinal

HS: hidradenitis suppurativa

MTX: methotrexate

NSAID: non-steroidal anti-inflammatory
drug

PsO: plaque psoriasis

PJIA: polyarticular juvenile idiopathic
arthritis

PsA: psoriatic arthritis

RA: rheumatoid arthritis

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
clindamycin (Cleocin [®]) + rifampin (Rifadin [®])	HS* clindamycin 300 mg PO BID and rifampin 300 mg PO BID	clindamycin: 1,800 mg/day rifampin: 600 mg/day
Cuprimine [®] (d-penicillamine)	RA* <u>Initial dose:</u> 125 or 250 mg PO QD <u>Maintenance dose:</u> 500 – 750 mg/day PO QD	1,500 mg/day
cyclosporine (Sandimmune [®] , Neoral [®])	PsO 2.5 mg/kg/day PO divided BID PsA* 2.5 – 3 mg/kg/day PO QD RA 2.5 – 4 mg/kg/day PO divided BID	PsO, RA: 4 mg/kg/day PsA: 3 mg/kg/day
doxycycline (Acticlate [®])	HS* 50 – 100 mg PO BID	300 mg/day
hydroxychloroquine (Plaquenil [®])	RA* <u>Initial dose:</u> 400 – 600 mg/day PO QD <u>Maintenance dose:</u> 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 PsA* 100 mg/day PO loading dose for 3 days followed by 20 mg/day PO QD RA 100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
methotrexate (Rheumatrex [®])	PsO	30 mg/week

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	<p>10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week</p> <p>PJIA* 10 – 20 mg/m²/week PO, SC, or IM</p> <p>PsA* 7.5 – 15 mg/week PO</p> <p>RA 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week</p>	
minocycline (Minocin [®])	HS* 50 – 100 mg PO BID	200 mg/day
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	AS, PsA Varies	Varies
Ridaura [®] (auranofin)	RA 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine [®])	<p>PJIA* 30-50 mg/kg/day PO divided BID</p> <p>PsA* 2 g/day PO QD</p> <p>RA 2 g/day PO in divided doses</p>	<p>PJIA: 2 g/day</p> <p>PsA: 5 g/day</p> <p>RA: 3 g/day</p>
Humira [®] (adalimumab)	<p>HS</p> <p><u>Initial dose:</u> 160 mg SC on Day 1, then 80 mg SC on Day 15</p> <p><u>Maintenance dose:</u> 40 mg SC once weekly starting on Day 29</p>	40 mg/week

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

- Contraindications:
 - Enbrel should not be administered to patients with sepsis.
- 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, pyoderma sinifica fistulans, Velpeau's disease, and Verneuil's disease."
 - In HS, Hurley stages are used to determine severity of disease. Hurley stage II indicates moderate disease, and is characterized by recurrent abscesses, with sinus tracts and scarring, presenting as single or multiple widely separated lesions. Hurley stage III indicates severe disease, and is characterized by diffuse or near-diffuse involvement presenting as multiple interconnected tracts and abscesses across an entire area.

V. 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	<i>Adults:</i> <u>Initial dose:</u> 50 mg SC twice weekly for 3 months <u>Maintenance dose:</u> 50 mg SC once weekly <i>Pediatrics:</i> Weight < 63 kg: 0.8 mg/kg SC once weekly Weight ≥ 63 kg: 50 mg SC once weekly	50 mg/week
HS	50 mg SC twice weekly	100 mg/week

VI. Product Availability

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

VII. References

1. Enbrel Prescribing Information. Thousand Oaks, CA: Immunex Corporation: November 2017. Available at http://pi.amgen.com/~/media/amgen/repositorysites/pi-amgen.com/enbrel/enbrel_pi.ashx. Accessed September 4, 2018.
2. Smolen JS, Landewé R, Breedveld FC, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2013 update. *Ann Rheum Dis*. 2014; 73: 492-509.
3. Singh JA, Furst DE, Bharat A, et al. 2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis. *Arthritis Care Res*. 2012; 64(5): 625-639.
4. Ringold, S, Weiss PF, et al. 2013 Update of the 2011 American College of Rheumatology recommendations for the treatment of juvenile idiopathic arthritis. *Arthritis Care Res*. 2013; 65 (10): 2499-2512.
5. Beukelman T, 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 & Research*, 2011;63(4):465-482.
6. 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.
7. Menter A, Gottlieb A, Feldman, SR, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis: Section 2. Psoriatic arthritis: overview and guidelines of care for treatment with an emphasis on the biologics. *J Am Acad Dermatol* May 2008; 58(5): 826-50.
8. Menter A, Korman, NJ, Elmets CA, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. *J Am Acad Dermatol*. 2009;60:643-659.
9. Menter A, Korman NF, Elmets cA, et al. American Academy of Dermatology. Guidelines of care for the management of psoriasis and psoriatic arthritis. Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol*. 10.1016/j.jaad.2009.03.027
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. Ward MM, 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 & Rheumatology*, 2015. DOI 10.1002/ART.39298.
12. Braun J, van den berg R, et al. 2010 Update of the ASAS/EULAR recommendations for the management of ankylosing spondylitis. *Am Rheu Dis*. 2011; 70; 896-904.
13. 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* 2015;0:1-12. doi:10.1136/annrheumdis-2015-208337

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
<p>Policy split from CP.PHAR.85.Psoriasis Treatments and CP.PHAR.86.Arthritis Treatments. RA, PJIA, PsA, AS, PsO: Removed criteria related to HBV, malignant disease, concomitant use with other biologics, and concurrent administration of live vaccines; added dosing requirement. PJIA: removed question related to number of affected joints; modified criteria to require trial of MTX, unless contraindicated; added sulfasalazine as an alternative to MTX if MTX is contraindicated.</p> <p>RA: changed age requirement to 18; modified criteria to require trial of MTX, unless contraindicated; added sulfasalazine and hydroxychloroquine as an alternative to MTX if MTX is contraindicated.</p> <p>PsO: removed duration of trial for topical and phototherapy. PsA: required trial of MTX and added requirement for the following if MTX cannot be used: leflunomide, cyclosporine, sulfasalazine & azathioprine.</p> <p>Re-auth: combined into All Indications; added dosing and reasons to discontinue; for PsO, changed efficacy criteria related to Psoriasis Area and Severity Index (PASI)-75 to general efficacy statement. Removed Otezla from list of therapies to trial per PDL. Modified approval duration to 6 months for initial and 12 months for renewal.</p>	06.16	08.16

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Changed age for plaque psoriasis to ≥ 4 to reflect changes in PI indication.	12.16	
Converted to new template. RA: Revised criteria for confirmation of diagnosis per 2010 ACR Criteria. PsO: Trial requirement modified to require the concomitant use of oral and topical or phototherapy. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs.	08.17	08.17
Converted to new template. Added new dosage form Enbrel Mini. Updated appendices and references.	12.08.17	
2Q 2018 annual review: policies combined for HIM and Medicaid lines of business; modified trial and failure for RA to at least one conventional DMARD; removed TB testing for all indications; modified max dose requirements to specify pediatric and adult-specific dosing for PJIA and PsO; removed specific diagnosis requirements for PsO; removed trial and failure of phototherapy and topical therapy for PsO; added off-label criteria for HS; references reviewed and updated.	02.27.18	05.18
4Q 2018 annual review: allowed bypassing conventional DMARDs for axial PsA and required trial of NSAIDs; updated dosing for off-label indications HS; references reviewed and updated.	09.04.18	11.18

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.

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.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene[®] and Centene Corporation[®] are registered trademarks exclusively owned by Centene Corporation.