Clinical Policy: Etanercept (Enbrel)

Reference Number: PA.CP.PHAR.250
Effective Date: 01/18
Last Review Date: 04/19 Revision Log

Coding Implications

Description
Etanercept (Enbrel®) is tumor necrosis factor 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 (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of Pennsylvania Health and Wellness® that Enbrel is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

1. Diagnosis of;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of methotrexate (MTX) at up to maximally indicated doses for ≥ 3 consecutive months, 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 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 effect are experienced;
5. Dose does not exceed 50 mg once weekly.

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 MTX at up to maximally indicated doses for ≥ 3 consecutive months, unless contraindicated or clinically significant adverse effects are experienced;
   b. If intolerance or contraindication to MTX (*see Appendix D*), failure of sulfasalazine or leflunomide for ≥ 3 consecutive months 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. Dose does not exceed 50 mg once weekly.

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 trialed for ≥ 4 weeks unless contraindicated or clinically significant adverse effects are experienced;
5. Dose does not exceed 50 mg once weekly.

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 PA.CP.PMN.53 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 Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to;

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 (1 or 2)**:**

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.

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

2. Refer to PA.CP.PMN.53 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 – PA.CP.PMN.53 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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
doxycycline (Acticlate®)	**HS*** 50 – 100 mg PO BID	300 mg/day
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/m^2/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
minocycline (Minocin®)	**HS*** 50 – 100 mg PO BID	200 mg/day
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS** Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
Humira® (adalimumab)	**HS** <u>Initial dose:</u> 160 mg SC on Day 1, then 80 mg SC on Day 15 <u>Maintenance dose:</u> 40 mg SC once weekly starting on Day 29	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, pyodermia 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.

- PsA: According to the 2018 American College of Rheumatology and National Psoriasis Foundation guidelines, TNF inhibitors or oral small molecules (e.g., methotrexate, sulfasalazine, cyclosporine, leflunomide, apremilast) are preferred over other biologics (e.g., interleukin-17 inhibitors or interleukin-12/23 inhibitors) for treatment-naïve disease. TNF inhibitors are also generally recommended over oral small molecules as first-line therapy unless disease is not severe, member prefers oral agents, or TNF inhibitor therapy is contraindicated.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RA PsA	25 mg SC twice weekly or 50 mg SC once weekly	50 mg/week
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 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	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 February 26, 2019.
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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

14. Singh JA, Guyatt G, Ogdie A, et al. 2018 American College of Rheumatology/National Psoriasis Foundation Guideline for the treatment of psoriatic arthritis. American College of Rheumatology. 2019; 71(1):5-32. doi: 10.1002/art.40726

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	Approval Date
2Q 2018 annual review: 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; added off-label criteria for HS; references reviewed and updated.	04.03.18	
2Q 2019 annual review: removed trial and failure requirement of conventional DMARDs (e.g., MTX)/NSAIDs for biologic DMARDs for PsA per ACR/NPF 2018 guidelines; references reviewed and updated.	04.17.19	