BlueCross BlueShield
Federal Employee Program

# ENBREL (etanercept) / ERELZI* (etanercept – szzs) / ETICOVO* (etanercept-ykro)

*These medications are included in this policy but are not available on the market as of yet

## RATIONALE FOR INCLUSION IN PA PROGRAM

### Background

Enbrel (etanercept) and its biosimilars are grouped within a class of medications called biologic response modifiers, or biologics. By working on the immune system, biologics block proteins that contribute to the disease process. Tumor necrosis factor (TNF) is a substance made by your body's immune system. People with inflammatory diseases such as rheumatoid arthritis (RA), plaque psoriasis (PsO), psoriatic arthritis (PsA), polyarticular juvenile idiopathic arthritis (pJIA), juvenile psoriatic arthritis (JPsA), and ankylosing spondylitis (AS) have excess TNF in their bodies. Enbrel and its biosimilars reduce levels of the active form of TNF. By limiting TNFα, Enbrel and its biosimilars have demonstrated efficacy in managing chronic inflammatory diseases (1).

### Regulatory Status

FDA-approved indications: Enbrel and its biosimilars are tumor necrosis factor (TNF) blockers indicated for the treatment of: (2-4)

Rheumatoid Arthritis (RA) - Enbrel and its biosimilars are 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 and its biosimilars can be initiated in combination with methotrexate (MTX) or used alone.

Polyarticular Juvenile Idiopathic Arthritis (pJIA) - Enbrel and its biosimilars are indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (pJIA) in patients aged 2 years or older.

Psoriatic Arthritis (PsA) – Enbrel and its biosimilars are indicated 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 and its biosimilars can be used in combination with methotrexate (MTX) in patients who do not respond adequately to MTX alone.

Juvenile Psoriatic Arthritis (JPsA) - Enbrel and its biosimilars are indicated for the treatment of active juvenile psoriatic arthritis (JPsA) in pediatric patients aged 2 years or older.

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Ankylosing Spondylitis (AS) – Enbrel and its biosimilars are indicated for reducing signs and symptoms in patients with active ankylosing spondylitis (AS).

Plaque Psoriasis (PsO) – Enbrel and its biosimilars are indicated 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.

Enbrel and its biosimilars carry boxed warnings regarding serious infections and malignancies. Because Enbrel and its biosimilars suppress the immune system, patients are at a greater risk for getting serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis), and infections due to other opportunistic pathogens. Lymphoma and other malignancies have been reported in children and adolescent patients treated with TNF blockers (2-4).

Patients should be screened for latent tuberculosis infection. Patients at risk for hepatitis B virus (HBV) infection should be evaluated for evidence of prior HBV infection. Hepatitis B virus carriers should be monitored for reactivation during and several months after therapy. Enbrel and its biosimilars should not be used in combination with other biologic agents. Enbrel and its biosimilars should not be initiated in patients with an active infection. Enbrel and its biosimilars should be discontinued if a patient develops a serious infection or sepsis during treatment (2-4).

Pancytopenia, aplastic anemia, lupus-like syndrome, anaphylaxis reactions, and congestive heart failure (new onset or worsening) may develop during Enbrel or its biosimilars therapy and therapy should be discontinued (2-4).

Use of Enbrel or its biosimilars with anakinra, abatacept, or cyclophosphamide is not recommended as the use may increase the risk of serious adverse events, including infections (2-4).

Off-Label Use:

There is sufficient medical literature to support the use of Enbrel or its biosimilars in adolescents for the treatment of rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) (3-

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10). Enbrel 25mg twice weekly dosing is supported by literature for patients who prefer that dosing method (11).

A study evaluating Enbrel in 3 subtypes of childhood arthritis (CLIPPER), has demonstrated efficacy of Enbrel among 122 patients with extended oligoarticular juvenile idiopathic arthritis (eoJIA), enthesitis-related arthritis (ERA), or psoriatic arthritis (PsA). The 12-week data analysis demonstrated that Enbrel was effective and well-tolerated in this combined group of patients (6).

Paller, et al. studied the same medication in children and found that Enbrel is both safe and effective to treat severe pediatric psoriasis. This was initially reported in the New England Journal of Medicine with follow-up in other journals (7-10).

**Summary**

Enbrel (etanercept) and its biosimilars are tumor necrosis factor (TNF) blockers indicated for the treatment of polyarticular juvenile idiopathic arthritis (pJIA), moderately to severely active rheumatoid arthritis (RA), active psoriatic arthritis (PsA), juvenile psoriatic arthritis (JPsA) active ankylosing spondylitis (AS), chronic moderate to severe plaque psoriasis (PsO) who are candidates for systemic therapy or phototherapy; with a negative test for latent TB infection or is receiving treatment or has completed treatment for latent TB, not at risk for HBV infection or HBV infection has been ruled out or treatment for HBV has been initiated, absent of active infection, and not taken in combination with another biologic agent (1-4).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Enbrel and its biosimilars while maintaining optimal therapeutic outcomes.

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