Enbrel

Description

Enbrel (etanercept), Erelzi (etanercept – szzs)

Background

Enbrel and Erelzi 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 (1).

Tumor necrosis factor (TNF) is a substance made by your body's immune system. People with inflammatory diseases such as rheumatoid arthritis, plaque psoriasis, psoriatic arthritis, juvenile idiopathic arthritis, and ankylosing spondylitis have too much TNF in their bodies. Enbrel and Erelzi reduce levels of the active form of TNF. By limiting TNFα, Enbrel and Erelzi have demonstrated efficacy in managing chronic inflammatory diseases (1).

Regulatory Status

FDA-approved indication: Enbrel and Erelzi are tumor necrosis factor (TNF) blockers indicated for the treatment of: (2-3)

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

Polyarticular Juvenile Idiopathic Arthritis (pJIA) - Enbrel and Erelzi 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 Erelzi 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 Erelzi can be used in combination with methotrexate (MTX) in patients who do not respond adequately to MTX alone.

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

Plaque Psoriasis (PsO) – Enbrel and Erelzi 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 Erelzi carry boxed warnings regarding serious infections and malignancies. Because Enbrel and Erelzi 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 (2-3).

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 Erelzi should not be used in combination with other biologic agents. Enbrel and Erelzi should not be initiated in patients with an active infection. Enbrel and Erelzi should be discontinued if a patient develops a serious infection or sepsis during treatment (2-3).

Pancytopenia, aplastic anemia, lupus-like syndrome, anaphylaxis reactions, and congestive heart failure (new onset or worsening) may develop during Enbrel or Erelzi therapy and therapy should be discontinued (2-3).

Use of Enbrel or Erelzi with anakinra, abatacept, or cyclophosphamide is not recommended as the use may increase the risk of serious adverse events, including infections (2-3).

Off-label use:
There is sufficient medical literature to support the use of Enbrel or Erelzi in adolescents for the treatment of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis (3-14).
An ongoing, Phase 3b, open-label, multicenter study is in progress (CLIPPER), which 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 (10).

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 (11-13).

**Related policies**
Actemra, Cimzia, Cosentyx, Humira, Kineret, Orenica, Remicade, Rituxan, Simponi, Stelara, Xeljanz

**Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Enbrel and Erelzi may be considered **medically necessary** in patients 2 years of age and older with moderately to severely active Polyarticular Juvenile Idiopathic Arthritis (JIA); in patients 2 years of age and older with chronic moderate to severe Plaque Psoriasis (PsO) who are candidates for systemic therapy or phototherapy; in patients 12 years of age and older with moderately to severely active Rheumatoid Arthritis (RA), Active Psoriatic Arthritis (PsA), Active Ankylosing Spondylitis (AS); 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 to be used in combination with any other biologic DMARD or targeted synthetic DMARD; not given concurrently with live vaccines.

Enbrel and Erelzi are considered **investigational** in patients with all other indications.

**Prior-Approval Requirements**

**Diagnoses**

Patient must have **ONE** of the following:

**Age** 2 years of age or older
1. Moderately to severely active Polyarticular Juvenile Idiopathic Arthritis (JIA)

**Age**: 4 years of age or older

1. Chronic moderate to severe Plaque Psoriasis (PsO)
   a. Inadequate response, intolerance, or contraindication to either conventional systemic therapy or phototherapy

**Age**: 12 years of age or older

1. Moderately to severely active Rheumatoid Arthritis (RA)
2. Active Psoriatic Arthritis (PsA)
3. Active Ankylosing Spondylitis (AS)

**AND ALL** of the following:

1. Result for latent TB infection is negative **OR** result was positive for latent TB and patient completed treatment (or is receiving treatment) for latent TB
2. Patient is not at risk for HBV infection **OR** patient is at risk for HBV infection and HBV infection has been ruled out or treatment for HBV infection has been initiated.
3. Absence of active infection (including tuberculosis and hepatitis B virus (HBV))
4. **NOT** to be used in combination with any other biologic DMARD or targeted synthetic DMARD
5. **NOT** given concurrently with live vaccines

### Prior – Approval Renewal Requirements

**Diagnoses**

Patient must have **ONE** of the following:

**Age**: 2 years of age or older

1. Polyarticular Juvenile Idiopathic Arthritis (JIA)

**Age**: 4 years of age or older

1. Plaque Psoriasis (PsO)
Age 12 years of age or older

1. Rheumatoid Arthritis (RA)
2. Psoriatic Arthritis (PsA)
3. Ankylosing Spondylitis (AS)
4. Plaque Psoriasis (PsO)

AND ALL of the following:
1. Condition has improved or stabilized with Enbrel or Erelzi
2. Absence of active infection (including tuberculosis and hepatitis B virus (HBV))
3. NOT to be used in combination with any other biologic DMARD or targeted synthetic DMARD
4. NOT given concurrently with live vaccines

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval Renewal Limits
Duration 18 months

Rationale

Summary
Enbrel and Erelzi are tumor necrosis factor (TNF) blocker indicated for the treatment of polyarticular juvenile idiopathic arthritis (JIA), moderately to severely active rheumatoid arthritis (RA), active psoriatic arthritis (PsA), 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.
Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Enbrel and Erelzi while maintaining optimal therapeutic outcomes.

References
