Learn more about ENBREL® in Psoriatic Arthritis

ENBREL is a soluble Tumor Necrosis Factor (TNF) receptor treatment that binds to TNF[1,2]

- Binds to and biologically inactivates TNF to decrease inflammation[1]
- ENBREL suppresses the immune system and may increase the risk of infections and other serious side effects.[1] See Important Safety Information on the inside spread

ENBREL provides significant and sustained improvements in clinical signs and symptoms and sustained inhibition of further joint damage[1]

- Among patients with PsA who received ENBREL, the clinical responses were apparent at the time of the first visit (4 weeks) and were maintained through 6 months of therapy[1]
- ENBREL is effective as monotherapy or in combination with MTX[1]

ENBREL helped patients achieve clearer skin[1]

- ENBREL can help improve skin lesions of psoriasis[1]
- ENBREL is effective as monotherapy or in combination with MTX[1]

ENBREL is a subcutaneous once-weekly 50-mg injection that can be administered alone or in combination with MTX[1]

ENBREL has a half-life of approximately 4.3 days[1]

- Following the last dose of ENBREL, approximately 50% of ENBREL will be cleared from the body in that time[3]
- Therefore, adhering to the ENBREL 50-mg weekly dosing regimen is important to maintain therapeutic serum concentrations to provide sustained efficacy[1,4]

Prescription ENBREL® (etanercept) is administered by injection

INDICATION

ENBREL is indicated for reducing signs and symptoms, keeping joint damage from getting worse, and improving physical function in patients with psoriatic arthritis. ENBREL can be used with or without methotrexate.

SELECTED SAFETY INFORMATION

ENBREL has been shown to increase the risk of 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, and should be discontinued if a patient develops a serious infection or sepsis. Test for latent TB (if positive, start treatment for TB prior to starting ENBREL) and monitor for active TB during treatment. Lymphoma and other malignancies, some fatal, have been reported in children and adolescents treated with tumor necrosis factor (TNF) blockers, including ENBREL.

See Important Safety Information (ISI) for additional information on the inside spread.

Enbrel®
etanercept

IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS

Patients treated with ENBREL are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids or were predisposed to infection because of their underlying disease. ENBREL should not be initiated in the presence of sepsis, active infections, or allergy to ENBREL or its components. ENBREL should be discontinued if a patient develops a serious infection or sepsis. Reported infections include: 1) Active tuberculosis (TB), including reactivation of latent TB. Patients with TB have frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before ENBREL use and periodically during therapy. Treatment for latent infection should be initiated prior to ENBREL use, 2) Invasive fungal infections, including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, and pneumocystosis. Patients with histoplasmosis or other invasive fungal infections may present with disseminated, rather than localized, disease. Antigen and antibody testing for histoplasmosis may be negative in some patients with active

infection. Empiric antifungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness, and 3) Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella and Listeria.

The risks and benefits of treatment with ENBREL should be carefully considered prior to initiating therapy in patients 1) with chronic or recurrent infection, 2) who have been exposed to TB, 3) who have resided or traveled in areas of endemic TB or endemic mycoses, or 4) with underlying conditions that may predispose them to infections such as advanced or poorly controlled diabetes. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with ENBREL, including the possible development of TB in patients who tested negative for latent TB prior to initiating therapy.

MALIGNANCIES

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor (TNF) blockers, including ENBREL.

In adult clinical trials of all TNF blockers, more cases of lymphoma were seen compared to control patients. The risk of lymphoma may be up to several-fold higher in PsA patients. The role of TNF blocker therapy in the development of malignancies is unknown.

Cases of acute and chronic leukemia have been reported in association with postmarketing TNF blocker use in PsA and other indications. The risk of leukemia may be higher in patients with PsA (approximately 2-fold) than the general population.

Melanoma and non-melanoma skin cancer (NMSC) have been reported in patients treated with TNF blockers, including ENBREL. Periodic skin examinations should be considered for all patients at increased risk for skin cancer.

Pediatric Patients

In patients who initiated therapy at ≤ 18 years of age, approximately half of the reported malignancies were lymphomas (Hodgkin's and non-Hodgkin's lymphoma). Other cases included rare malignancies usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents. Most of the patients were receiving concomitant immunosuppressants.

NEUROLOGIC REACTIONS

Treatment with TNF-blocking agents, including ENBREL, has been associated with rare (< 0.1%) cases of new onset or exacerbation of central nervous system demyelinating disorders, some presenting with mental status changes and some associated with permanent disability, and with peripheral nervous system demyelinating disorders. Cases of transverse myelitis, optic neuritis, multiple sclerosis, Guillain-Barré syndromes, other peripheral demyelinating neuropathies, and new onset or exacerbation of seizure disorders have been reported in postmarketing experience with ENBREL therapy. Prescribers should exercise caution in considering the use of ENBREL in patients with preexisting or recent-onset central or peripheral nervous system demyelinating disorders.

CONGESTIVE HEART FAILURE

Cases of worsening congestive heart failure (CHF) and, rarely, new-onset cases have been reported in patients taking ENBREL. Caution should be used when using ENBREL in patients with CHF. These patients should be carefully monitored.

HEMATOLOGIC REACTIONS

Rare cases of pancytopenia, including aplastic anemia, some fatal, have been reported. The causal relationship to ENBREL therapy remains unclear. Exercise caution when considering ENBREL in patients who have a previous history of significant hematologic abnormalities. Advise patients to seek immediate medical attention if they develop signs or symptoms of blood dyscrasias or infection. Consider discontinuing ENBREL if significant hematologic abnormalities are confirmed.

HEPATITIS B REACTIVATION

Reactivation of hepatitis B has been reported in patients who were previously infected with hepatitis B virus (HBV) and received concomitant TNF-blocking agents, including ENBREL. Most reports occurred in patients also taking immunosuppressive agents, which may contribute to hepatitis B reactivation. Exercise caution when considering ENBREL in these patients.

ALLERGIC REACTIONS

Allergic reactions associated with administration of ENBREL during clinical trials have been reported in < 2% of patients. If an anaphylactic reaction or other serious allergic reaction occurs, administration of ENBREL should be discontinued immediately and appropriate therapy initiated.

IMMUNIZATIONS

Live vaccines should not be administered to patients on ENBREL. Pediatric patients, if possible, should be brought up to date with all immunizations prior to initiating ENBREL. In patients with exposure to varicella virus, temporarily discontinue ENBREL and consider prophylactic treatment with Varicella Zoster Immune Globulin.

AUTOIMMUNITY

Autoantibodies may develop with ENBREL, and rarely lupus-like syndrome or autoimmune hepatitis may occur. These may resolve upon withdrawal of ENBREL. Stop ENBREL if lupus-like syndrome or autoimmune hepatitis develops.

WEGENER'S GRANULOMATOSIS PATIENTS

The use of ENBREL in patients with Wegener's granulomatosis receiving immunosuppressive agents (eg, cyclophosphamide) is not recommended.

MODERATE TO SEVERE ALCOHOLIC HEPATITIS

Based on a study of patients treated for alcoholic hepatitis, exercise caution when using ENBREL in patients with moderate to severe alcoholic hepatitis.

ADVERSE REACTIONS

The most commonly reported adverse reactions in PsA clinical trials were injection site reaction and infection. In clinical trials of all other adult indications, adverse reactions were similar to those reported in PsA clinical trials.

DRUG INTERACTIONS

The use of ENBREL in patients receiving concurrent cyclophosphamide therapy is not recommended. The risk of serious infection may increase with concomitant use of abatacept therapy. Concurrent therapy with ENBREL and anakinra is not recommended. Hypoglycemia has been reported following initiation of ENBREL therapy in patients receiving medication for diabetes, necessitating a reduction in anti-diabetic medication in some of these patients.

Please see accompanying Prescribing Information and Medication Guide or click here for Prescribing Information and Medication Guide

Enbrel®
etanercept

Learn more about ENBREL® in Psoriatic Arthritis, continued

ENBREL can be stored at room temperature for up to 14 days with protection from light, sources of heat, and humidity[1]

- ENBREL should be refrigerated at 36°F to 46°F (2°C to 8°C)[1]
- Once ENBREL has been stored at room temperature, it should not be placed back into the refrigerator[1]
- If not used within 14 days at room temperature, ENBREL should be discarded[1]
- Do not store ENBREL in extreme heat or cold. DO NOT FREEZE[1]

ENBREL in Pregnancy[1]

- Studies with ENBREL during pregnancy do not support an association between ENBREL and major birth defects. Clinical registry* data showed that the proportion of patients with major birth defects was higher with ENBREL, however differences in disease severity may have impacted the occurrence of birth defects
- The risk of fetal/neonatal adverse reactions with in utero ENBREL is unknown. Consider the risks and benefits prior to administering live or live-attenuated vaccines to infants exposed to ENBREL in utero. ENBREL is present in cord blood in infants born to mothers administered ENBREL during pregnancy
- Limited data show that ENBREL is present in low levels in human milk and minimally absorbed by the breastfed infant. The benefits of breastfeeding should be considered along with the mother's clinical need for ENBREL and any potential adverse effects on the breastfed child from the drug or from the underlying maternal condition

Prescription ENBREL® (etanercept) is administered by injection

INDICATION

ENBREL is indicated for reducing signs and symptoms, keeping joint damage from getting worse, and improving physical function in patients with psoriatic arthritis. ENBREL can be used with or without methotrexate.

SELECTED SAFETY INFORMATION

ENBREL has been shown to increase the risk of 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, and should be discontinued if a patient develops a serious infection or sepsis. Test for latent TB (if positive, start treatment for TB prior to starting ENBREL) and monitor for active TB during treatment. Lymphoma and other malignancies, some fatal, have been reported in children and adolescents treated with tumor necrosis factor (TNF) blockers, including ENBREL.

See Important Safety Information (ISI) for additional information on the inside spread.

References: 1. Enbrel® (etanercept) Prescribing Information, Immunex Corporation, Thousand Oaks, Calif. November 2016. **2.** Scallon B, Cai A, Solowski N, et al. Binding and functional comparison of two types of tumor necrosis factor antagonists. *J Pharmacol Exp Ther.* 2002;301:418-426. **3.** Bauer LA. Clinical pharmacokinetics and pharmacodynamics. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, eds. *Pharmacotherapy: A Pathophysiologic Approach.* 8th ed. New York, NY: McGraw-Hill; 2011:1-47. **4.** Keystone EC, Schiff MH, Kremer JM, et al. Once-weekly administration of 50 mg etanercept in patients with active rheumatoid arthritis: results of a multicenter, randomized, double-blind, placebo-controlled trial. *Arthritis Rheum.* 2004;50:353-363.

*The OTIS registry and Scandinavian study

 USA-916-81622

Enbrel® etanercept