Enbrel® etanercept

MOVING FORWARD BY PUTTING PATIENTS FIRST

ENBREL MINI® SINGLE-DOSE PREFILLED CARTRIDGE WITH AUTOTOUCH® REUSABLE AUTOINJECTOR

GETTING STARTED WITH ENBREL MINI® WITH AUTOTOUCH®

Prescription ENBREL is administered by injection.

INDICATION

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. ENBREL can be initiated in combination with methotrexate or used alone.

IMPORTANT SAFETY CONSIDERATIONS

ENBREL suppresses the immune system and has been associated with **serious and sometimes fatal infections, including opportunistic infections and TB**. Other serious and sometimes fatal adverse reactions including **malignancies**, neurologic reactions, congestive heart failure, hematologic reactions, hepatitis B reactivation, allergic reactions, lupus-like syndrome and autoimmune hepatitis have also been reported. ENBREL is contraindicated in patients with sepsis. The most commonly reported adverse reactions in RA clinical trials were injection site reaction and infection.

Please see additional indications and Important Safety Information on back, and accompanying Prescribing Information and Medication Guide.

GETTING STARTED WITH ENBREL MINI® WITH AUTOTOUCH®

The provided checklist can help you ensure that patients with their newly prescribed Enbrel Mini® with AutoTouch® start and stay on track.

Share the following brochure with your patients:

Enbrel Mini® with AutoTouch® Brochure

- Learn more about the features of the AutoTouch® and how they were designed from patient insights
- See link to demo video of Enbrel Mini® with AutoTouch®
- Discover the variety of ways *ENBREL Support*® is ready to help

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Did you know:
ENBREL collaborates with CoverMyMeds® to provide an electronic prior authorization (ePA) solution and live support when needed*

CHECK OFF EACH ITEM BEFORE YOUR PATIENT LEAVES THE OFFICE:

- ☐ Give your patient an AutoTouch® in the office, or use AutoTouch® Direct for home delivery†
- ☐ Provide injection training in office to ensure your patient is able to use Enbrel Mini® with AutoTouch®‡
- ☐ Offer to start the *ENBREL Support*® enrollment process for your patient
- ☐ Tear off the bottom portion and give it to your patient along with the ENBREL Medication Guide

Did you know: you can watch the Enbrel Mini® with AutoTouch® demonstration video with your patient. Visit EnbrelMini.com

*Amgen, the manufacturer of ENBREL, has entered into a fee for service arrangement with CoverMyMeds® to provide a streamlined ePA experience after you have chosen to prescribe ENBREL.
†After completed form is validated by the dispensing pharmacy, AutoTouch® will be shipped directly to the patient.
‡It is important that you thoroughly review the Instructions for Use. These instructions cover everything you need to know about how to use Enbrel Mini® with AutoTouch®.

CONGRATULATIONS!
YOU AND YOUR DOCTOR HAVE DECIDED ON ENBREL MINI® WITH AUTOTOUCH®

Enbrel® etanercept

Let's get started:

- Enroll in *ENBREL Support*® today
  - Call 1-888-4ENBREL (1-888-436-2735)
  - Be sure to save the number in your phone
- Look out for a call from your specialty pharmacy — they will talk to you about scheduling your ENBREL delivery
- Visit EnbrelSupport.com to download the ENBREL Patient Roadmap

QUESTIONS? CALL *ENBREL SUPPORT*® AT 1-888-4ENBREL (1-888-436-2735), Monday-Sunday from 8 AM to 11 PM (ET)

Please read the attached Medication Guide for ENBREL.

Medication Guide

Enbrel® (en-brel) (etanercept) injection, for subcutaneous use

Enbrel® (en-brel) (etanercept) for injection, for subcutaneous use

Read the Medication Guide that comes with Enbrel before you start using it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your healthcare provider about your medical condition or treatment. It is important to remain under your healthcare provider's care while using Enbrel. Enbrel is a prescription medicine called a Tumor Necrosis Factor (TNF) blocker that affects your immune system.

What is the most important information I should know about Enbrel?

Enbrel may cause serious side effects, including:

1. Risk of Infection
2. Risk of Cancer

1. Risk of infection

Enbrel can lower the ability of your immune system to fight infections. Some people have serious infections while taking Enbrel. These infections include tuberculosis (TB), and infections caused by viruses, fungi, or bacteria that spread throughout their body. Some people have died from these infections.

- Your healthcare provider should test you for TB before starting Enbrel.
- Your healthcare provider should monitor you closely for symptoms of TB during treatment with Enbrel even if you tested negative for TB.
- Your healthcare provider should check you for symptoms of any type of infection before, during, and after your treatment with Enbrel.

You should not start taking Enbrel if you have any kind of infection unless your healthcare provider says it is okay.

2. Risk of cancer

- There have been cases of unusual cancers, some resulting in death, in children and teenage patients who started using TNF-blocking agents at less than 18 years of age.
- For children, teenagers, and adults taking TNF-blocker medicines, including Enbrel, the chances of getting lymphoma or other cancers may increase.
- People with rheumatoid arthritis, especially those with very active disease, may be more likely to get lymphoma.

Before starting Enbrel, be sure to talk to your healthcare provider:

Enbrel may not be right for you. Before starting Enbrel, tell your healthcare provider about all of your medical conditions, including:

Infections. Tell your healthcare provider if you:

- have an infection. See "**What is the most important information I should know about Enbrel?**"
- are being treated for an infection.
- think you have an infection.
- have symptoms of an infection such as fever, sweats or chills, cough or flu-like symptoms, shortness of breath, blood in your phlegm, weight loss, muscle aches, warm, red or painful areas on your skin, sores on your body, diarrhea or stomach pain, burning when you urinate or urinating more often than normal, and feel very tired.
- have any open cuts on your body.
- get a lot of infections or have infections that keep coming back.
- have diabetes, HIV, or a weak immune system. People with these conditions have a higher chance for infections.
- have TB, or have been in close contact with someone with TB.
- were born in, lived in, or traveled to countries where there is a risk for getting TB. Ask your healthcare provider if you are not sure.
- live, have lived in, or traveled to certain parts of the country (such as the Ohio and Mississippi River valleys, or the Southwest) where there is a greater risk for getting certain kinds of fungal infections (histoplasmosis, coccidioidomycosis, blastomycosis). These infections may happen or become more severe if you use Enbrel. Ask your healthcare provider if you do not know if you live or have lived in an area where these infections are common.
- have or have had hepatitis B.

Also, before starting Enbrel, tell your healthcare provider:

- **About all the medicines you take including prescription and over-the-counter medicines, vitamins and herbal supplements including:**
  - **Orencia (abatacept) or Kineret (anakinra).** You have a higher chance for serious infections when taking Enbrel with Orencia or Kineret.
  - **Cyclophosphamide (Cytoxan).** You may have a higher chance for getting certain cancers when taking Enbrel with cyclophosphamide.
  - **Anti-diabetic medicines.** If you have diabetes and are taking medication to control your diabetes, your healthcare provider may decide you need less anti-diabetic medicine while taking Enbrel.

Keep a list of all your medications with you to show your healthcare provider and pharmacist each time you get a new medicine. Ask your healthcare provider if you are not sure if your medicine is one listed above.

Other important medical information you should tell your healthcare provider before starting Enbrel, includes if you:

- have or had a nervous system problem such as multiple sclerosis or Guillain-Barré syndrome.
- have or had heart failure.
- are scheduled to have surgery.
- have recently received or are scheduled to receive a vaccine.
  - All vaccines should be brought up-to-date before starting Enbrel.
  - People taking Enbrel should not receive live vaccines.
  - Ask your healthcare provider if you are not sure if you received a live vaccine.
- are allergic to rubber or latex.
  - The needle covers on the single-dose prefilled syringes, the needle covers within the white caps on the single-dose prefilled SureClick autoinjectors, and within the purple caps of the Enbrel Mini cartridges contain dry natural rubber.
- have been around someone with varicella zoster (chicken pox).
- are pregnant or plan to become pregnant. It is not known if Enbrel will harm your unborn baby. If you took Enbrel during pregnancy, talk to your healthcare provider prior to administration of live vaccines to your infant.
- are breastfeeding or plan to breastfeed. Enbrel can pass into breast milk. Talk to your healthcare provider about the best way to feed your baby while taking Enbrel.

See the section "**What are the possible side effects of Enbrel?**" below for more information.

What is Enbrel?

Enbrel is a prescription medicine called a Tumor Necrosis Factor (TNF) blocker.

Enbrel is used to treat:

- **moderately to severely active rheumatoid arthritis (RA).** Enbrel can be used alone or with a medicine called methotrexate.
- **moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) in children ages 2 years and older.**
- **psoriatic arthritis (PsA).** Enbrel can be used alone or with methotrexate.
- **ankylosing spondylitis (AS).**
- **chronic moderate to severe plaque psoriasis (PsO) in children 4 years and older and adults** who may benefit from taking injections or pills (systemic therapy) or phototherapy (ultraviolet light).

You may continue to use other medicines that help treat your condition while taking Enbrel, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and prescription steroids, as recommended by your healthcare provider.

Enbrel can help reduce joint damage and the signs and symptoms of the above-mentioned diseases. People with these diseases have too much of a protein called tumor necrosis factor (TNF), which is made by your immune system. Enbrel can reduce the effect of TNF in the body and block the damage that too much TNF can cause, but it can also lower the ability of your immune system to fight infections. See "**What is the most important information I should know about Enbrel?**" and "**What are the possible side effects of Enbrel?**"

Who should not use Enbrel?

Do not use Enbrel if you:

- have an infection that has spread through your body (sepsis).

How should I use Enbrel?

- Enbrel is given as an injection under the skin (subcutaneous or SC).
- If your healthcare provider decides that you or a caregiver can give the injections of Enbrel at home, you or your caregiver should receive training on the right way to prepare and inject Enbrel. Do not try to inject Enbrel until you have been shown the right way by your healthcare provider or nurse.
- Enbrel is available in the forms listed below. Your healthcare provider will prescribe the type that is best for you.
  - Single-dose Prefilled Syringe
  - Single-dose Prefilled SureClick Autoinjector
  - Multiple-dose Vial
  - Enbrel Mini single-dose cartridge for use with the AutoTouch reusable autoinjector
- See the detailed "Instructions for Use" with this Medication Guide for instructions about the right way to store, prepare, and give your Enbrel injections at home.
- Your healthcare provider will tell you how often you should use Enbrel. Do not miss any doses of Enbrel. If you forget to use Enbrel, inject your dose as soon as you remember. Then, take your next dose at your regular(ly) scheduled time. In case you are not sure when to inject Enbrel, call your healthcare provider or pharmacist. **Do not use Enbrel more often than as directed by your healthcare provider.**
- Your child's dose of Enbrel depends on his or her weight. Your child's healthcare provider will tell you which form of Enbrel to use and how much to give your child.

What are the possible side effects of Enbrel?

Enbrel can cause serious side effects, including:

- See "**What is the most important information I should know about Enbrel?**"
- **Infections.** Enbrel can make you more likely to get infections or make any infection that you have worse. Call your healthcare provider right away if you have any symptoms of an infection. See **"Before starting Enbrel, be sure to talk to your healthcare provider"** for a list of symptoms of infection.
- **Previous Hepatitis B infection.** If you have been previously infected with the hepatitis B virus (a virus that affects the liver), the virus can become active while you use Enbrel. Your healthcare provider may do a blood test before you start treatment with Enbrel and while you use Enbrel.
- **Nervous system problems.** Rarely, people who use TNF-blocker medicines have developed nervous system problems such as multiple sclerosis, seizures, or inflammation of the nerves of the eyes. Tell your healthcare provider right away if you get any of these symptoms: numbness or tingling in any part of your body, vision changes, weakness in your arms and legs, and dizziness.
- **Blood problems.** Low blood counts have been seen with other TNF-blocker medicines. Your body may not make enough of the blood cells that help fight infections or help stop bleeding. Symptoms include fever, bruising or bleeding very easily, or looking pale.
- **Heart failure including new heart failure or worsening of heart failure you already have.** New or worse heart failure can happen in people who use TNF-blocker medicines like Enbrel. If you have heart failure your condition should be watched closely while you take Enbrel. Call your healthcare provider right away if you get new or worsening symptoms of heart failure while taking Enbrel, such as shortness of breath or swelling of your lower legs or feet.
- **Psoriasis.** Some people using Enbrel developed new psoriasis or worsening of psoriasis they already had. Tell your healthcare provider if you develop red scaly patches or raised bumps that may be filled with pus. Your healthcare provider may decide to stop your treatment with Enbrel.
- **Allergic reactions.** Allergic reactions can happen to people who use TNF-blocker medicines. Call your healthcare provider right away if you have any symptoms of an allergic reaction. Symptoms of an allergic reaction include a severe rash, a swollen face, or trouble breathing.
- **Autoimmune reactions, including:**
  - **Lupus-like syndrome.** Symptoms include a rash on your face and arms that gets worse in the sun. Tell your healthcare provider if you have this symptom. Symptoms may go away when you stop using Enbrel.
  - **Autoimmune hepatitis.** Liver problems can happen in people who use TNF-blocker medicines, including Enbrel. These problems can lead to liver failure and death. Call your healthcare provider right away if you have any of these symptoms: feel very tired, skin or eyes look yellow, poor appetite or vomiting, pain on the right side of your stomach (abdomen).

Common side effects of Enbrel include:

- **Injection site reactions** such as redness, swelling, itching, or pain. These symptoms usually go away within 3 to 5 days. If you have pain, redness, or swelling around the injection site that does not go away or gets worse, call your healthcare provider.
- **Upper respiratory infections** (sinus infections).

These are not all the side effects with Enbrel. Tell your healthcare provider about any side effect that bothers you or does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store Enbrel?

- Store Enbrel in the refrigerator between 36°F to 46°F (2°C to 8°C).
- Store Enbrel in the original carton to protect from light or damage.
- If needed, you may store the Enbrel prefilled syringe, SureClick autoinjector, Enbrel Mini cartridge, or the dose tray for the multi-dose vial at room temperature between 68°F to 77°F (20°C to 25°C) for up to 14 days.
  - Once Enbrel has reached room temperature, do not put it back in the refrigerator.
- Throw away Enbrel that has been stored at room temperature after 14 days.
- Mixed Enbrel multi-dose vial should be used right away or kept in the refrigerator between 36°F to 46°F (2°C to 8°C) for up to 14 days.
- **Do not** store Enbrel in extreme heat or cold such as in your vehicle's glove box or trunk.
- **Do not freeze.**
- **Do not shake.**
- **Keep Enbrel and all medicines out of the reach of children.**

General information about the safe and effective use of Enbrel.

Medicines are sometimes prescribed for purposes not mentioned in a Medication Guide. Do not use Enbrel for a condition for which it was not prescribed. Do not give Enbrel to other people, even if they have the same condition. It may harm them.

This Medication Guide summarizes the most important information about Enbrel. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about Enbrel that was written for healthcare professionals.

What are the ingredients in Enbrel?

Single-dose Prefilled Syringe, Single-dose Prefilled SureClick Autoinjector, and Enbrel Mini single-dose cartridge:

Active Ingredient: etanercept

Inactive Ingredients: L-arginine hydrochloride, sodium chloride, and sucrose

Multiple-dose Vial:

Active Ingredient: etanercept

Inactive Ingredients: mannitol, sucrose, tromethamine

AMGEN®

Manufactured by: Immunex Corporation, Thousand Oaks, CA 91320-1799, U.S. License Number 1132

For more information, call 1 888 4ENBREL (1 888 436 2735).

This Medication Guide has been approved by the U.S. Food and Drug Administration. Revised: 05/2018

INDICATIONS

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. ENBREL can be initiated in combination with methotrexate or used alone.

ENBREL is indicated for reducing signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis in patients ages 2 and older.

ENBREL is indicated for reducing signs and symptoms, inhibiting the progression of structural damage of active arthritis, and improving physical function in patients with psoriatic arthritis. ENBREL can be used with or without methotrexate.

ENBREL is indicated for reducing signs and symptoms in patients with active ankylosing spondylitis.

ENBREL is indicated for the treatment of patients 4 years or older with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.

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 RA 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 RA and other indications. The risk of leukemia may be higher in patients with RA (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 RA clinical trials were injection site reaction and infection. In clinical trials of all other adult indications, adverse reactions were similar to those reported in RA clinical trials.

In general, the adverse reactions in pediatric patients were similar in frequency and type as those seen in adult patients. The types of infections reported in pediatric patients were generally mild and consistent with those commonly seen in the general pediatric population.

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 inside pocket.

AMGEN®

Manufactured by Immunex Corporation
Marketed by Amgen Inc.
Thousand Oaks, CA 91320

www.enbrel.com

Enbrel® etanercept