Your doctor is the best resource for medical advice and information. The health information contained herein is provided for educational / awareness purposes only and is not intended to replace discussions with a medical practitioner and/or medical advice or be construed as a promotional information.

Package Leaflet: Information for the user
ETANERCEPT Solution for Injection
in 25 mg Pre-filled Syringe &
50 mg Pre-filled Pen
ENBREL®

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- If you have any further questions, ask your doctor.
- This medicine has been prescribed for you or a child in your care. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours or those of the child you are caring for.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What ENBREL (Etanercept) is and what it is used for

ENBREL (Etanercept) is a medicine that is made from two human proteins. It blocks the activity of another protein in the body that causes inflammation. ENBREL (Etanercept) works by reducing the inflammation associated with certain diseases.

- Reduction in signs and symptoms of moderately to severely active rheumatoid arthritis in patients who have had an inadequate response to one or more disease modifying anti-rheumatic drugs.
- Moderately to severely active early rheumatoid arthritis and juvenile rheumatoid arthritis.
- Treatment of ankylosing spondylitis in adults who have had inadequate therapy response to conventional therapy.

- For reduction in signs and symptoms of active arthritis in patients with psoriatic arthritis.
- Treatment of adult patients with chronic moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
- Treatment of chronic severe plaque psoriasis in children and adolescents from the age of 8 years who are inadequately controlled by, or are intolerant to other systemic therapies or photo therapies.

2. What you need to know before you use ENBREL (Etanercept)

Do not use ENBREL (Etanercept)

- If you, or the child you are caring for, are allergic to etanercept or any of the other ingredients of ENBREL (Etanercept) (listed in section 6).
- If you or the child you are caring for, experience allergic reactions such as chest tightness, wheezing, dizziness or rash, do not inject more ENBREL (Etanercept), and contact your doctor immediately.
- If you or the child you are caring for, have or are at risk of developing a serious blood infection called sepsis. If you are not sure, please contact your doctor.
- If you or the child you are caring for, have an infection of any kind. If you are not sure, please talk to your doctor.

Warning and precautions

Talk to your doctor before taking ENBREL (Etanercept).

- **Allergic reactions**: If you or the child you are caring for, experience allergic reactions such as chest tightness, wheezing, dizziness or rash, do not inject more ENBREL (Etanercept), and contact your doctor immediately.
- **Infections/surgery:** If you or the child you are caring for, develop a new infection, or are about to have any major surgery, your doctor may wish to monitor the treatment with ENBREL (Etanercept).
- **Infections/diabetes:** Tell your doctor if you or the child you are caring for, have a history of recurrent infections or suffer from diabetes or other conditions that increase the risk of infection.
- **Infections/monitoring:** Tell your doctor of any recent travel. If you or the child you are caring for, develops symptoms of an infection such as fever, chills or cough, notify your doctor immediately. Your doctor may decide to continue to monitor you or the child for the presence of infections after you or the child stop using ENBREL (Etanercept).
- **Tuberculosis:** As cases of tuberculosis have been reported in patients treated with ENBREL (Etanercept), your doctor will check for signs and symptoms of tuberculosis before starting ENBREL (Etanercept). This may include a thorough medical history, a chest X-ray and a tuberculin test. The conduct of these tests should be recorded on the Patient Card. It is very important that you tell your doctor if you or the child you are caring for, have ever had tuberculosis, or have been in close contact with someone who has had tuberculosis. If symptoms of tuberculosis (such as persistent cough, weight loss, listlessness, mild fever), or any other infection appear during or after therapy, tell your doctor immediately.
- **Hepatitis B:** Tell your doctor if you or the child you are caring for, have or have ever had hepatitis B. Your doctor should test for the presence of hepatitis B infection before you or the child begin treatment with ENBREL (Etanercept). Treatment with ENBREL (Etanercept) may result in reactivation of hepatitis B in patients who have previously been infected with the hepatitis B virus. If this occurs, you should stop using ENBREL (Etanercept).

- **Hepatitis C:** Tell your doctor if you or the child you are caring for, have hepatitis C. Your doctor may wish to monitor the treatment with ENBREL (Etanercept) in case the infection worsens.
- **Blood disorders:** Seek medical advice immediately if you or the child you are caring for, have any signs or symptoms such as persistent fever, sore throat, bruising, bleeding or paleness. Such symptoms may point to the existence of potentially life-threatening blood disorders, which may require discontinuation of ENBREL (Etanercept).
- **Nervous system and eye disorders:** Tell your doctor if you or the child you are caring for, have multiple sclerosis, optic neuritis (inflammation of the nerves of the eyes) or transverse myelitis (inflammation of the spinal cord). Your doctor will determine if ENBREL (Etanercept) is an appropriate treatment.
- **Congestive heart failure:** Tell your doctor if you or the child you are caring for, have a history of congestive heart failure, because ENBREL (Etanercept) needs to be used with caution under these circumstances.
- **Cancer:** Tell your doctor if you have or have ever had lymphoma (a type of blood cancer) or any other cancer before you are given ENBREL (Etanercept).
  Patients with severe rheumatoid arthritis, who have had the disease for a long time, may be at higher than average risk of developing lymphoma.
  Children and adults taking ENBREL (Etanercept) may have an increased risk of developing lymphoma or another cancer.
  Some children and teenage patients who have received ENBREL (Etanercept) or other medicines that work the same way as ENBREL (Etanercept) have developed cancers, including unusual types, which sometimes resulted in death.
  Some patients receiving ENBREL (Etanercept) have developed skin cancers. Tell your doctor if you or the child develop any change in the appearance of the skin or growths on the skin.
- **Chickenpox:** Tell your doctor if you or the child you are caring for, are exposed to chickenpox when using ENBREL (Etanercept). Your doctor will determine if preventive treatment for chickenpox is appropriate.
- **Latex:** The needle cover is made from latex (dry natural rubber). Contact your doctor before using ENBREL (Etanercept) if the needle cover will be handled by, or ENBREL (Etanercept) will be given to, someone with a known or possible hypersensitivity (allergy) to latex.
- **Alcohol abuse**: ENBREL (Etanercept) should not be used for the treatment of hepatitis related to alcohol abuse. Please tell your doctor if you or the child in your care have a history of alcohol abuse.
- **Wegener's granulomatosis**: ENBREL (Etanercept) is not recommended for the treatment of Wegener's granulomatosis, a rare inflammatory disease. If you or the child in your care have Wegener's granulomatosis, talk to your doctor.
- **Anti-diabetic medicines**: Tell your doctor if you or the child you are caring for, have diabetes or are taking medicines to treat diabetes. Your doctor may decide if you or the child need less anti-diabetic medicine while taking ENBREL (Etanercept).

Children and adolescents

Vaccinations: If possible, children should be up to date with all vaccinations before using ENBREL (Etanercept). Some vaccines, such as oral polio vaccine, should not be given while using ENBREL (Etanercept). Please consult your doctor before you or the child you are caring for, receive any vaccines.

Inflammatory bowel disease (IBD): There have been cases of IBD in patients with juvenile idiopathic arthritis (JIA) treated with Etanercept. Tell the doctor if the child you are caring for, develops any abdominal cramps and pain, diarrhoea, weight loss or blood in the stool.

ENBREL (Etanercept) should not normally be used in children with polyarthritis or extended oligoarthritis below the age of 2 years, or in children with enthesitis-related arthritis or psoriatic arthritis below the age of 12 years, or in children with psoriasis below the age of 8 years.

Other medicines and ENBREL (Etanercept)

Tell your doctor if you or the child under your care are taking, have recently taken or might take any other medicines (including anakinra, abatacept or sulfasalazine), even those not prescribed by the doctor. You or the child should not use ENBREL (Etanercept) with medicines that contain the active substance anakinra or abatacept.

Pregnancy and breast-feeding

ENBREL (Etanercept) should only be used during pregnancy if clearly needed. You should consult your doctor if you become pregnant, think you may be pregnant, or are planning to have a baby.

If you received ENBREL (Etanercept) during pregnancy, your baby may have a higher risk of getting an infection. In addition, one study found more birth defects when the mother had received ENBREL (Etanercept) in pregnancy, compared with mothers who had not received ENBREL (Etanercept) or other similar medicines (TNF-antagonists), but there was no particular kind of birth defect reported. Another study found no increased risk of birth defects when the mother had received ENBREL (Etanercept) in pregnancy. Your doctor will help you to decide whether the benefits of treatment outweigh the potential risk to your baby. It is important that you tell the baby's doctors and other healthcare professionals about the use of ENBREL (Etanercept) during pregnancy before the baby receives any vaccine (for more information see section 2, "Vaccinations").

Women using ENBREL (Etanercept) should not breast-feed, since ENBREL (Etanercept) passes into human breast milk.

Driving and using machines

The use of ENBREL (Etanercept) is not expected to affect the ability to drive or use machines.

ENBREL (Etanercept) contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially 'sodium-free'.

3. How to use ENBREL (Etanercept)

Enbrel (Etanercept) is available in dosage of 25 mg & 50 mg. Always use this medicine exactly as the doctor has told you. Check with the doctor if you are not sure.

If you feel that the effect of ENBREL (Etanercept) is too strong or too weak, talk to your doctor.

Dosing for adult patients (aged 18 years or over)

Rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis

The usual dose is 25 mg given twice a week or 50 mg once a week as an injection under the skin. However, your doctor may determine an alternative frequency at which to inject ENBREL (Etanercept).

Plaque psoriasis

The usual dose is 25 mg twice a week or 50 mg once a week.

Alternatively, 50 mg may be given twice a week for up to 12 weeks, followed by 25 mg twice a week or 50 mg once a week.

Your doctor will decide how long you should take ENBREL (Etanercept) and whether retreatment is needed based on your response. If ENBREL (Etanercept) has no effect on your condition after 12 weeks, your doctor may tell you to stop taking this medicine.

Use in children and adolescents

The appropriate dose and frequency of dosing for the child or adolescent will depend on body weight and disease. Your doctor will determine the correct dose for the child and will prescribe an appropriate strength of ENBREL (Etanercept) (25 mg or 50 mg).

For psoriasis in patients from the age of 8 years, the usual dose is 0.8 mg of ENBREL (Etanercept) per kg bodyweight (up to a maximum of 50 mg), and should be given once weekly. If ENBREL (Etanercept) has no effect on the child's condition after 12 weeks, your doctor may tell you to stop using this medicine.

The recommended dose for Juvenile idiopathic arthritis is 0.4 mg/kg (up to a maximum of 25 mg per dose), given twice weekly as a subcutaneous injection with an interval of 3-4 days between doses or 0.8 mg/kg (up to a maximum of 50 mg per dose) given once weekly. Discontinuation of treatment should be considered in patients who show no response after 4 months.

The doctor will provide you with detailed directions for preparing and measuring the appropriate dose.

Method and route of administration

ENBREL (Etanercept) is administered by an injection under the skin (by subcutaneous injection).

ENBREL (Etanercept) can be taken with or without food or drink.

"Instructions for preparing and giving an injection of ENBREL (Etanercept)".

Do not mix the ENBREL (Etanercept) solution with any other medicine.

To help you remember, it may be helpful to write in a diary which day(s) of the week ENBREL (Etanercept) should be used.

If you use more ENBREL (Etanercept) than you should

If you have used more ENBREL (Etanercept) than you should (either by injecting too much on a single occasion or by using it too frequently), talk to a doctor immediately. Always have the outer carton of the medicine with you, even if it is empty.

If you forget to inject ENBREL (Etanercept)

If you forget a dose, you should inject it as soon as you remember, unless the next scheduled dose is the next day; in which case you should skip the missed dose. Then continue to inject the medicine on the usual day(s). If you do not remember until the day that the next injection is due, do not take a double dose (two doses on the same day) to make up for a forgotten dose.

If you stop using ENBREL (Etanercept)

Your symptoms may return upon discontinuation.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Allergic reactions

If any of the following happen, do not inject more ENBREL (Etanercept). Tell your doctor immediately, or go to the casualty department at your nearest hospital.

- Trouble swallowing or breathing
- Swelling of the face, throat, hands, or feet
- Feeling nervous or anxious, throbbing sensations, sudden reddening of the skin and/or a warm feeling
- Severe rash, itching, or hives (elevated patches of red or pale skin that often itch)

Serious allergic reactions are rare. However, any of the above symptoms may indicate an allergic reaction to ENBREL (Etanercept), so you should seek immediate medical attention.

Serious side effects

If you notice any of the following, you or the child may need urgent medical attention.

- Signs of **serious infections**, such as high fever that may be accompanied by cough, shortness of breath, chills, weakness, or a hot, red, tender, sore area on the skin or joints
- Signs of **blood disorders**, such as bleeding, bruising, or paleness
- Signs of **nerve disorders**, such as numbness or tingling, changes in vision, eye pain, or onset of weakness in an arm or leg
- Signs of **heart failure** or **worsening heart failure**, such as fatigue or shortness of breath with activity, swelling in the ankles, a feeling of fullness in the neck or abdomen, night-time shortness of breath or coughing, bluish colour of the nails or the lips
- Signs of **cancers:** Cancers may affect any part of the body including the skin and blood, and possible signs will depend on the type and location of the cancer. These signs may include weight loss, fever, swelling (with or without pain), persistent cough, presence of lumps or growths on the skin

- Signs of **autoimmune reactions** (where antibodies are made that may harm normal tissues in the body) such as pain, itching, weakness, and abnormal breathing, thinking, sensation, or vision
- Signs of lupus or lupus-like syndrome, such as weight changes, persistent rash, fever, joint or muscle pain, or fatigue
- Signs of **inflammation of the blood vessels** such as pain, fever, redness or warmth of the skin, or itching.

These are rare or uncommon side effects, but are serious conditions (some of which may rarely be fatal). If these signs occur, tell your doctor immediately, or visit the casualty department at your nearest hospital.

The known side effects of ENBREL (Etanercept) include the following in groups of decreasing frequency:

- **Very common** (may affect more than 1 in 10 people):
  Infections (including colds, sinusitis, bronchitis, urinary tract infections and skin infections); injection site reactions (including bleeding, bruising, redness, itching, pain, and swelling) (these do not occur as often after the first month of treatment; some patients have developed a reaction at an injection site that was recently used); and headache.

- **Common** (may affect up to 1 in 10 people):
  Allergic reactions; fever; rash; itching; antibodies directed against normal tissue (autoantibody formation).

- **Uncommon** (may affect up to 1 in 100 people):
  Serious infections (including pneumonia, deep skin infections, joint infections, blood infection, and infections at various sites); worsening of congestive heart failure; low red blood cell count, low white blood cell count, low neutrophil (a type of white blood cell) count; low blood platelet count; skin cancer (excluding melanoma); localised swelling of the skin (angioedema); hives (elevated patches of red or pale skin that often itch); eye inflammation; psoriasis (new or worsening); inflammation of the blood vessels affecting multiple organs; elevated liver blood tests (in patients also receiving methotrexate treatment, the frequency of elevated liver blood tests is common); abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems).

- **Rare** (may affect up to 1 in 1,000 people):
  Serious allergic reactions (including severe localised swelling of the skin and wheezing); lymphoma (a type of blood cancer); leukaemia (cancer affecting the blood and bone marrow); melanoma (a type of skin cancer); combined low platelet, red, and white blood cell count; nervous system disorders (with severe muscle weakness and signs and symptoms similar to those of multiple sclerosis or inflammation of the nerves of the eyes or spinal cord); tuberculosis; new onset congestive heart failure; seizures; lupus or lupus-like syndrome (symptoms may include persistent rash, fever, joint pain, and tiredness); skin rash, which may lead to severe blistering and peeling of the skin; lichenoid reactions (itchy reddish-purple skin rash and/or threadlike white-grey lines on mucous membranes); inflammation of the liver caused by the body's own immune system (autoimmune hepatitis; in patients also receiving methotrexate treatment, the frequency is uncommon); immune disorder that can affect the lungs, skin and lymph nodes (sarcoidosis); inflammation or scarring of the lungs (in patients also receiving methotrexate treatment, the frequency of inflammation or scarring of the lungs is uncommon).

- **Very rare** (may affect up to 1 in 10,000 people): failure of the bone marrow to produce crucial blood cells.

- **Not known** (frequency cannot be estimated from the available data): Merkel cell carcinoma (a type of skin cancer); Kaposi's sarcoma (a rare cancer related to infection with human herpes virus 8. Kaposi's sarcoma most commonly appear as purple lesions on the skin); excessive activation of white blood cells associated with inflammation (macrophage activation syndrome); recurrence of hepatitis B (a liver infection); worsening of a condition called dermatomyositis (muscle inflammation and weakness with an accompanying skin rash).

Side effects in children and adolescents

The side effects and their frequencies seen in children and adolescents are similar to those described above.

5. How to store and handle ENBREL (Etanercept)

ENBREL (Etanercept) pre-filled syringe and pre-filled pen must be stored refrigerated at 2°C to 8°C.

Do not freeze.

Keep the pre-filled syringes and pre-filled pens in the outer carton in order to protect from light.

Keep out of reach of children.

The needle cover of the pre-filled syringe, the needle cap of the pre-filled pen contains latex (dry natural rubber). Patients or caregivers should contact their doctor before using ENBREL (Etanercept) if the needle cover will be handled by or if ENBREL (Etanercept) will be given to someone with a known or possible hypersensitivity (allergy) to latex.

Patients or caregivers who are to administer ENBREL (Etanercept) must be instructed in proper syringe and needle disposal, and be cautioned against reuse of these items.

Unused ENBREL (Etanercept), syringes, or waste materials should be disposed of according to local requirements.

6. Contents of the pack and other information

List of Excipients

The excipients in the pre-filled syringe, pre-filled pen are sucrose, sodium chloride, L-arginine hydrochloride, sodium dihydrogen phosphate (sodium phosphate monobasic monohydrate), disodium hydrogen phosphate (sodium phosphate dibasic dihydrate), and water for injection.

Pre-filled syringe

Clear glass syringe (type I glass) with stainless steel needle, rubber needle cover and plastic plunger. The needle cover contains dry natural rubber (latex) (see section 2).

ENBREL (Etanercept) is single use pre-filled syringes of etanercept (25 mg).

ENBREL (Etanercept) 25 mg pre-filled syringes are available in a carton in 2's pack with alcohol swabs.

Pre-filled pen

Pre-filled pen containing clear type 1 glass pre-filled syringe with a stainless steel 27-gauge needle, rubber needle cover, and plastic plunger. The needle cap of the pre-filled pen contains dry natural rubber [latex].

ENBREL (Etanercept) is single-use pre-filled syringe in MYCLIC® pen contains etanercept (50 mg). ENBREL (Etanercept) 50 mg MYCLIC® pre-filled pens are available in a carton in 2's pack with alcohol swabs.

Manufacturer:

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