PATIENT INFORMATION LEAFLET

Serious infections, including tuberculosis (TB) may occur with ENBREL; some have resulted in death. Speak to your doctor at once if you develop any new infection while you take ENBREL. You may need to stop treatment if you develop an infection.

SCHEDULING STATUS: S4

ENBREL® 25 mg powder and solvent for solution for injection

Etanercept

Contains sugar

Each vial of ENBREL 25 mg powder and solvent for solution for injection contains 40 mg of mannitol and 10 mg of sucrose

Read all of this leaflet carefully before you are given ENBREL

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- ENBREL has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What ENBREL is and what it is used for
2. What you need to know before you use ENBREL
3. How to use ENBREL
4. Possible side effects
5. How to store ENBREL
6. Contents of the pack and other information

1. What ENBREL is and what it is used for

ENBREL is a biological medicine and is a type of protein called tumour necrosis factor (TNF) blocker that blocks the action of TNF in your body's immune system. People with an auto immune disease have too much TNF in

their bodies. ENBREL blocks the action of TNF, helping to treat your disease. But, in doing so, ENBREL lowers the ability of your immune system to fight infections.

ENBREL is an anti-rheumatic medicine used to treat:

- The signs and symptoms of active rheumatoid arthritis (RA) in adults and children. It is reserved for patients who have not responded to or have responded poorly to other disease-modifying medicines (DMARDS) used for rheumatoid arthritis. ENBREL can be used alone or in combination with methotrexate.
- Severe, active and progressive rheumatoid arthritis in adults not previously treated with methotrexate.
- Polyarticular-course juvenile idiopathic arthritis in children and adolescents from the age of 2 years, when the response to one or DMARDS has proved inadequate.
- Polyarticular-course juvenile idiopathic arthritis and extended oligoarthritis in children and adolescents from the age of 2 years when treatment with methotrexate has not worked well enough or is not suitable for them.
- Psoriatic arthritis in adolescents from the age of 12 years when treatment with methotrexate has not worked well enough or is not suitable for them.
- Enthesitis-related arthritis in adolescents from the age of 12 years when other widely used treatments have not worked well enough or are not suitable for them.
- The signs and symptoms of psoriatic arthritis (PS), and for inhibiting the progression of structural damage of active arthritis in patients. ENBREL can be used in combination with methotrexate in patients who do not respond adequately to methotrexate alone.
- Adults with a type of arthritis called ankylosing spondylitis (AS), and where your doctor may or may not be able to see swelling in the sacroiliac (pelvic) joints and/or your spine using X-rays and in patients where other widely used treatments have not worked well enough or are not suitable for them.
- Adults (aged 18 and over), for treatment of chronic moderate to severe plaque psoriasis, who are candidates for systemic therapy or phototherapy.
- Chronic severe plaque psoriasis in children and adolescents, (from the age of 6 years), who have had an inadequate response to, or are unable to take phototherapies or other systemic therapies.

RA, PS and AS are inflammatory diseases that can affect the joints in your body. Psoriasis is an inflammatory disease that affects the skin and can cause raised, thick, red and scaly patches (psoriatic skin lesions) that can occur anywhere in the body. Psoriatic arthritis is usually seen in patients with psoriasis and affects both the

joints and the skin.

2. What you need to know before you use ENBREL

Do not use ENBREL:

- if you are hypersensitive (allergic) to etanercept or to any of the other ingredients of ENBREL (listed in section 6)
- if you have or are at risk of sepsis (blood poisoning)
- if you have an infection of any type including tuberculosis or chronic infections and local infections (such as a leg ulcer)

Warnings and precautions

Take special care with ENBREL:

- if you are prone to infection (i.e. if you think you have an infection, are being treated for an infection, have signs of an infection such as fever, cough, flu-like symptoms and have open sores on your body). ENBREL may lessen the body's ability to fight infections. You should be evaluated for infections, specifically for tuberculosis before, during and after treatment with ENBREL.
- if you are about to have any surgery or if you develop a new infection.
- if you have any immune system disorders, cancer, advanced or poorly controlled diabetes mellitus (sugar diabetes). ENBREL may lessen the body's ability to fight infection.
- if you have tuberculosis (TB), or if you have been in close contact with someone who has had tuberculosis
- if you have or have had hepatitis B or hepatitis C
- if you have liver disease caused by the excessive intake of alcohol
- if you have or have ever had lymphoma (a type of blood cancer) or any other cancer. Patients with severe rheumatoid arthritis, who have had the disease for a long time, may be at higher than average risk of developing lymphoma. There have been reports of children and adolescents developing cancers, including lymphoma and skin cancers who have received ENBREL or other medicines that work in the same way as ENBREL. Tell your doctor if you or your child develops any change in the appearance of the skin or growths on the skin
- if you have any blood disorders (signs include persistent fever, bruising, bleeding, or paleness). ENBREL may increase the risk of blood disorders such as anaemia. There have been rare reports of serious blood

disorders, some resulting in death

- do not have any vaccinations (immunisations) without your doctor's approval
- if you have any diseases of the central nervous system such as multiple sclerosis, seizures, or optic neuritis (inflammation of the nerves of the eyes). ENBREL may make these conditions worse
- if you have any heart problems. ENBREL may worsen congestive heart failure
- if you are being treated for diabetes, as ENBREL may lower your blood sugar levels. ENBREL has been tested in elderly patients (65 – 87 years of age) with similar response rates and safety profiles as seen in adult patients under 65 years of age

Other medicines and ENBREL

Always tell your health care provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

ENBREL should NOT be used together with

- live attenuated vaccines, such as the oral polio vaccine
- anakinra as it may increase the risk of serious infection and blood disorders
- abatacept as it may increase the incidence of serious adverse events
- sulfasalazine as it may decrease your white blood cell count
- any other medicine in the same vial or syringe

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before using this medicine.

You should only be treated with ENBREL during pregnancy if clearly needed. It is important that you tell your health care provider about the use of ENBREL during pregnancy before the baby receives any vaccine.

You should only be treated with ENBREL during breastfeeding if clearly needed. Talk to your doctor if you want to breastfeed while on ENBREL treatment. It is important that you tell your baby's doctors and other health care providers about the use of ENBREL during breastfeeding before your baby receives any vaccine.

Safety in pregnancy and lactation has not been established.

Driving and using machines

No studies on the effects on the ability to drive and use machines have been performed.

It is not always possible to predict to what extent ENBREL may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which ENBREL affects them.

ENBREL contains latex

The rubber closure of the solvent syringe contains latex (dry natural rubber) and may cause severe allergic reactions. Patients or caregivers with a known or possible hypersensitivity (allergy) to latex should contact their doctor before using ENBREL.

ENBREL contains sugar

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before takin this medicine.

3. How to use ENBREL

Do not share medicines prescribed for you with any other person.

Always use ENBREL exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. To help you remember, write in a diary which days of the week you should have an injection. Your doctor will prescribe the appropriate dose for you or your child according to the condition.

Your doctor will tell you how long your treatment with ENBREL will last. Do not stop treatment early. If you have the impression that the effect of ENBREL is too strong or too weak, tell your doctor or pharmacist.

Adults

The usual adult dose of ENBREL for rheumatoid arthritis is 25 mg given twice a week (3 – 4 days apart) or 50 mg given once weekly, and can be administered as follows

- once weekly (two 25 mg injections reconstituted in 1,0 mL of water for injection) administered subcutaneously at approximately the same time, or
- one single 25 mg injection reconstituted in 1,0 mL of water for injection administered twice weekly, 3 – 4 days apart (i.e. two 25 mg single dose vials), or

If you have psoriatic arthritis, ankylosing spondylitis or non-radiographic axial spondylarthritis, the recommended dose is 50 mg per week (given as one single 25 mg injection reconstituted in 1,0 mL of water for injection given twice weekly, 3 – 4 days apart). Doses other than 25 mg administered twice weekly have not been studied.

If you have plaque psoriasis, the recommended starting dose of ENBREL for adult patients is 50 mg per week (given as one single 25 mg injection reconstituted in 1,0 mL water for injection administered twice weekly, 3 – 4 days apart. After three months your doctor will tell you whether to reduce your dose.

Children

The recommended dose of ENBREL for children with juvenile rheumatoid arthritis, idiopathic arthritis and psoriasis is based upon the child's body weight. Your child's doctor will tell you the amount of ENBREL your child should use.

See your doctor at regular visits. It is important that your doctor checks your progress to make sure that this medicine is working properly.

Route of administration

ENBREL is injected under the skin. Your doctor will show you how and where to give the injection. ENBREL must first be dissolved with 1 mL of the supplied water for injection. Follow the detailed instructions on ENBREL injection preparation and injection procedure as provided below.

The prepared ENBREL solution should be colourless to slightly yellow or pale brown, clear to slightly opalescent.

Do not use the solution if it is discoloured or cloudy or if it contains any lumps, flakes or particles. Some white foam may however remain in the vial.

Instructions for preparing and giving an ENBREL injection

a. Introduction

The following instructions explain how to prepare and inject ENBREL. Please read the instructions carefully and follow them step by step. You will be instructed by your doctor or his/ her assistant on the technique of self-injection. Do not attempt to self-inject an injection until you are sure that you understand how to prepare and give the injection.

This injection should not be mixed in the same syringe or vial with any other medicine.

b. Setting up for an injection

- Wash your hands thoroughly.
- Select a clean well-lit, flat working surface.
- The dose tray should contain the items listed below. (If not, do not use the dose tray and consult your pharmacist). Use only the items listed. Do NOT use any other syringe.
  - 1 x ENBREL vial
  - 1 x Pre-filled syringe containing clear, colourless solvent (water for injections)
  - 1 x Needle
  - 1 x Vial adaptor
  - 2 x alcohol swabs
- Inspect the expiry dates on both the vial label and the syringe label. They should not be used after the month and year shown.

c. Preparing the ENBREL dose for injection

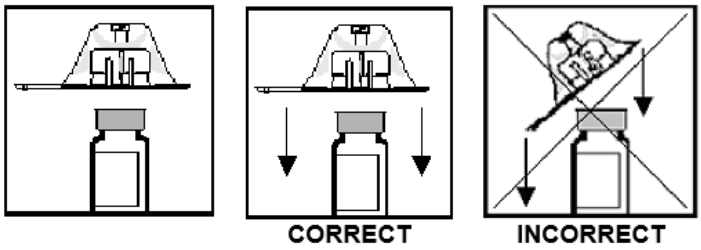
- Remove the contents of the tray
- Remove the plastic cap from the ENBREL vial (see Diagram 1). DO NOT remove the grey stopper or aluminium ring around the top of the vial.

Diagram 1



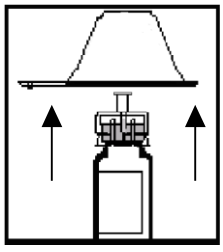
- Use a new alcohol swab to clean the grey stopper on the ENBREL vial. After cleaning, do not touch the stopper with your hands or allow it to touch any surface.
- Place the vial upright on a clean, flat surface.
- Remove the paper backing from the vial adaptor package.
- While still in the plastic package, place the vial adaptor on top of the ENBREL vial so that the vial adaptor spike is centred within the raised circle on top of the vial stopper (see Diagram 2).
- Hold the vial firmly on the flat surface with one hand. With the other hand, push STRAIGHT DOWN FIRMLY on the adaptor package until you feel the adaptor spike penetrate the vial stopper and FEEL AND HEAR THE ADAPTOR RIM LOCK INTO PLACE (see Diagram 3). Do not push down the adaptor at an angle (see Diagram 4). It is important that the vial adaptor spike completely penetrates the vial stopper.

Diagram 2. Diagram 3. Diagram 4.



- While holding the vial in one hand, remove the plastic packaging from the vial adaptor (see Diagram 5).

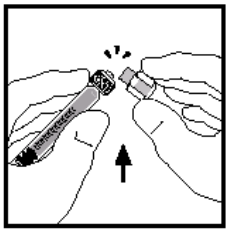
Diagram 5



- Remove the protective cover from the syringe tip by breaking the white cap along the perforation. This is done by holding the collar of the white cap while grasping the end of the white cap with the other hand and bending it down and then up until it is broken (see Diagram 6). DO NOT REMOVE THE WHITE COLLAR

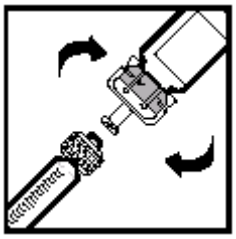
THAT REMAINS ON THE SYRINGE.

Diagram 6



- Do not use the syringe if this perforation is already broken. Start again with another dose tray.
- Holding the glass barrel of the syringe (not the white collar) in one hand, and the vial adaptor (not the vial) in the other, connect the syringe to the vial adaptor by inserting the tip into the opening and turn clockwise until completely secured (see Diagram 7).

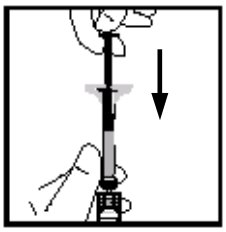
Diagram 7



d. Adding solvent

- While holding the vial upright on the flat surface, push the plunger VERY SLOWLY until all the solvent is in the vial. This will help to reduce foaming (lots of bubbles) (see Diagram 8).
- Once the solvent is added to the ENBREL, the plunger may move up by itself. This is due to air pressure and should not be of concern.

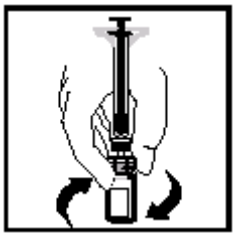
Diagram 8



- With the syringe still attached, gently move the vial in circles a few times, to dissolve the powder (see Diagram 9). DO NOT shake the vial. Wait until all the powder dissolves (usually less than 10 minutes). The solution should be clear and colourless to slightly yellow or pale brown, with no lumps, flakes, or particles.

Some white foam may remain in the vial this is normal. DO NOT use ENBREL if all the powder in the vial is not dissolved within 10 minutes. Start again with another dose tray.

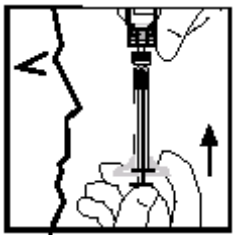
Diagram 9



e. Withdrawing the ENBREL solution from the vial

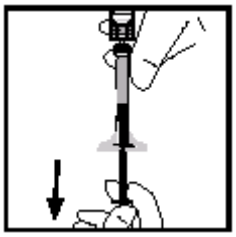
- With the syringe still attached to the vial and vial adaptor, hold the vial upside down at eye level. Push the plunger all the way into the syringe (see Diagram 10).

Diagram 10



- Then, slowly pull the plunger back to draw the liquid into the syringe (see Diagram 11). For adult patients, withdraw the entire volume. For children, remove only the portion of liquid as directed by your child's doctor. After you have withdrawn the ENBREL from the vial, you may have some air in the syringe. Do not be concerned as you will remove the air in a later step.

Diagram 11



- With the vial held upside down, unscrew the syringe from the vial adaptor by turning it anti-clockwise (see Diagram 12).

Diagram 12



- Place the filled syringe on the clean, flat surface. Make sure that the tip does not touch anything. Be careful not to push down on the plunger.

(Note: After you have completed these steps, a small amount of liquid may remain in the vial. This is normal.)

f. Placing the needle on the syringe

- The needle has been placed in a plastic container to keep it sterile.
- To open the plastic container, hold the short, wide end in one hand. Place your other hand on the longer portion of the container.
- To break the seal, bend the larger end down and then up until broken (see Diagram 13).

Diagram 13



- Once the seal has been broken, remove the short, wide end of the plastic container.
- The needle will remain in the long part of the package.
- While holding the needle and container in one hand, pick up the syringe and insert the syringe tip into the needle opening.
- Attach the syringe to the needle by turning it clockwise until completely secured (see Diagram 14).

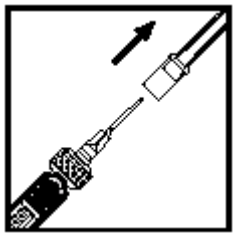
Diagram 14



- Remove the needle cover by firmly pulling it straight off the syringe, taking care not to touch the needle or

allow the needle to touch any surfaces (see Diagram 15). Be careful not to bend or twist the cover during removal to avoid damage to the needle.

Diagram 15



- While holding the syringe upright, remove any air bubbles by slowly pushing on the plunger until the air is removed (see Diagram 16).

Diagram 16



g. Choosing an injection site

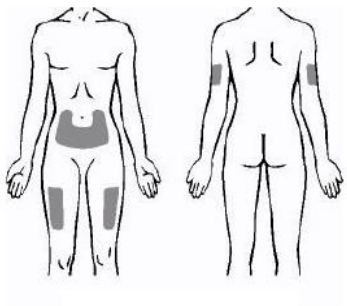
The three recommended injection sites for ENBREL include:

(1) the front of the middle thighs

(2) the abdomen, except for the 5 cm area right around the navel; and

(3) the outer area of the upper arms (see Diagram 17). If you are self injecting, you should not use the outer area of the upper arms.

Diagram 17



- A different site should be used for each new injection. Each new injection should be given at least 3 cm from

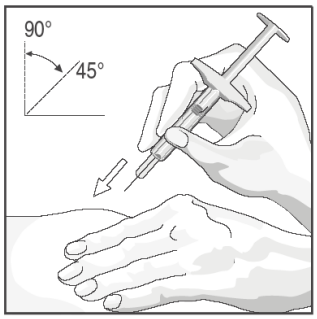
an old site. DO NOT inject into areas where the skin is tender, bruised, red, or hard. Avoid areas with scars or stretch marks. (It may be helpful to keep notes on the location of the previous injections.)

- If you or the child has psoriasis, you should try not to inject directly into any raised, thick, red, or scaly skin patches (‘psoriasis skin lesions’).

h. Preparing the injection site and injecting the ENBREL solution

- Wipe the injection site where ENBREL is to be injected with an alcohol swab, using a circular motion. DO NOT touch this area again before giving the injection.
- When the cleaned area of skin has dried, pinch and hold it firmly, with one hand. With the other hand, hold the syringe like a pencil.
- With a quick, short motion, push the needle all the way into the skin at an angle between 45 ° and 90 ° (see Diagram 18). With experience, you will find the angle that is most comfortable for you or the child. Be careful not to push the needle into the skin too slowly, or with great force.

Diagram 18



- When the needle is completely inserted into the skin, release the skin that you are holding.
- With your free hand, hold the syringe near its base to stabilize it. Then slowly push the plunger to inject all of the solution at a slow steady rate (see Diagram 19).

Diagram 19



- When the syringe is empty, remove the needle from the skin being careful to keep it at the same angle it was

when it was inserted.

- Press a cotton ball over the injection site for 10 seconds. Slight bleeding may occur. DO NOT rub the injection site. A bandage is optional.

i. Disposing of supplies

- The syringe and needles should NEVER be reused. Dispose of the needles and syringe as instructed by your doctor, nurse or pharmacist.
- **All questions should be answered by a doctor, nurse or pharmacist familiar with ENBREL.**

If you inject more ENBREL than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

If you forget to inject ENBREL

If you forget to give yourself an injection, inject the next dose as soon as you remember. Then go back to your normal dosing schedule. However, if it is nearly time for your next dose, skip the missed dose and carry on using the medicine as before. Do not use a double dose to make up for forgotten individual doses.

4. Possible side effects

ENBREL can have side effects.

Not all side effects reported for ENBREL are included in this leaflet. Should your general health worsen or if you experience any untoward effects while using ENBREL, please consult your health care provider for advice.

If any of the following happens, stop using ENBREL and tell your doctor immediately or go to the casualty department at your nearest hospital

- Serious allergic reactions such as a tight chest, wheezing, dizziness, fast heartbeat, difficulty swallowing, swelling of the face, eyelids or around the eyes, lips or tongue and skin rash
- Signs of blood disorders such as unusual bleeding, bruising or paleness especially if fever and sore throat are also present

- Signs of serious infections, such as high fever that may be accompanied by a cough, shortness of breath, chills, weakness, or a hot, red, tender, sore area on the skin or joints

These are all very serious side effects. If you have them, you may have had a serious reaction to ENBREL. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following

Frequent side effects

- infections such as respiratory infections (cough, fever, chills, sneezing, congestion, sore throat), kidney infections (frequent or painful urination) or skin infections (skin rash, redness, swelling or itching of skin). You should be evaluated for infections before, during and after treatment
- autoimmune reactions where antibodies are made that may harm the normal tissues in the body
- general itching of the skin, rash
- reactions at the injection site including redness, bleeding, bruising, itching, swelling or pain at the place of injection or previously used site
- fever or chills

Less frequent side effects

- serious infections (including pneumonia, deep skin infections, joint infections, blood infection, infections at various sites and infections caused by parasites)
- tuberculosis, opportunistic infections, (including fungal, bacterial and viral infections)
- melanoma and non-melanoma skin cancers
- low blood platelet count, low red blood cell count, low white blood cell count, low neutrophil (a type of white blood cell) count, failure of the bone marrow to produce crucial blood cells
- inflammation of the blood vessels affecting multiple organs
- serious allergic reactions (including severe localised swelling of the skin, wheezing)
- an immune disorder that can affect the lungs, skin and lymph nodes (sarcoidosis)
- 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)

- seizure (fit)
- inflammation of the eye
- new onset or worsening of existing congestive heart failure including shortness of breath or troubled breathing, chest pain, numbness on one side of the face or body
- inflammation or scarring of the lungs
- elevated liver blood tests, inflammation of the liver caused by the body's own immune system (autoimmune hepatitis)
- localised swelling of the skin (angioedema)
- psoriasis (new or worsening),
- hives (elevated patches of red or pale skin that often itch)
- extreme sensitivity reaction resulting in inflammation and damage to the blood vessels mainly in the skin.
- lupus-like syndrome (symptoms may include persistent rash, fever, pain or back pain, joint or muscle pain or stiffness, loss of energy and tiredness)

Side effects where the frequency is unknown

- recurrence of hepatitis B (a liver infection)
- *Listeria* (infections caused by certain types of bacteria)
- lymphoma (a type of blood cancer)
- leukaemia (cancer affecting the blood and bone marrow)
- Merkel cell carcinoma (a type of skin cancer)
- a condition where your body stops producing new blood cells (aplastic anaemia)
- histiocytosis haematophagic (excessive activation of white blood cells associated with inflammation)
- headache
- a condition where the immune system attacks the nerves (Guillain-Barré syndrome)
- inflammation of the nerves which can result in loss in sensation, tingling and pain, difficulty walking and weakness, numbness
- pain from nerve damage which can cause muscle weakening and wasting to be experienced
- abdominal cramps and pain, diarrhoea, weight loss or blood in the stool (signs of bowel problems)

- painful red or purplish rash that can cause blistering or peeling of the skin. These may be signs of lupus erythematosus or Stevens-Johnson Syndrome, or toxic epidermal necrolysis (TEN)
- damage to the tiny filters inside your kidneys leading to poor kidney function (glomerulonephritis)

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor or pharmacist. You can also report side effects to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. By reporting side effects, you can help provide more information on the safety of ENBREL.

You can report any suspected adverse drug reactions associated with the use of the medicine directly to Pfizer via ZAF.AEReporting@pfizer.com

5. How to store ENBREL

- Store all medicines out of reach of children
- Store ENBREL in the refrigerator (2 – 8 °C). DO NOT FREEZE
- Reconstituted solutions of ENBREL should be administered as soon as possible after preparation. If not administered immediately after preparation, the ENBREL prepared solution may be stored in the vial in the refrigerator (2 – 8 °C) for up to 6 hours
- Return all unused medicine to your pharmacist
- Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets)

6. Contents of the pack and other information

What ENBREL contains

- ENBREL is supplied as a powder with a solvent for solution for injection.
- The powder contains the active substance etanercept 25 mg.
- The other ingredients are mannitol, sucrose and trometamol.
- The solvent for solution for injection is provided in a pre-filled syringe and contains 1 mL water for injection.

What ENBREL looks like and contents of the pack

Before the preparation of the solution, the powder in the vial forms a white cake. After preparation of the solution, the liquid is colourless to slightly yellow or pale brown, clear to slightly opalescent.

ENBREL is supplied in a carton containing two dose trays each with two divisions. Each dose tray contains one 25 mg single-use vial of ENBREL, a pre-filled clear glass syringe with a tamper evident seal, a needle-free transfer device (vial adapter) and two alcohol swabs.

Holder of Certificate of Registration

Pfizer Laboratories (Pty) Ltd

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Sandton 2196

South Africa

Tel: +27(0)11 320 6000 / 0860 734 937 (Toll-free South Africa)

This leaflet was last revised in

12 November 2025

Registration number

ENBREL 25 mg: 34/3.1/0330

Solvent for ENBREL 25 mg: 34/34/0331