

PACKAGE LEAFLET: INFORMATION FOR THE USER

Enbrel 50 mg solution for injection in pre-filled pen Etanercept

Read all (both sides) of this leaflet carefully before you start using this medicine.

- Keep this leaflet. You may need to read it again.
- Your doctor will also give you a Patient Alert Card, which contains important safety information that you need to be aware of before and during treatment with Enbrel.
- If you any have further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you are concerned about any side effect, or if you notice any side effects that are not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

Information in this leaflet is organised under the following 7 sections:

1. **What Enbrel is and what it is used for**
2. **Before you use Enbrel**
3. **How to use Enbrel**
4. **Possible side effects**
5. **How to store Enbrel**
6. **Further information**
7. **Using the MYCLIC pre-filled pen to inject Enbrel (See overleaf)**

1. WHAT ENBREL IS AND WHAT IT IS USED FOR

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

In adults (aged 18 and over), Enbrel can be used for moderate or severe **rheumatoid arthritis**, **psoriatic arthritis**, severe **ankylosing spondylitis** and moderate or severe **psoriasis** – in each case usually when other widely used treatments have not worked well enough or are not suitable for you.

For rheumatoid arthritis, Enbrel is usually used in combination with methotrexate, although it may also be used alone if treatment with methotrexate is unsuitable for you. Whether used alone or in combination with methotrexate, Enbrel can slow down the damage to your joints caused by the rheumatoid arthritis and improve your ability to do normal daily activities.

For psoriatic arthritis patients with multiple joint involvement, Enbrel can improve your ability to do normal daily activities. For patients with multiple symmetrical painful or swollen joints (e.g., hands, wrists and feet), Enbrel can slow down the structural damage to those joints caused by the disease.

Enbrel is also prescribed for the treatment of severe psoriasis in patients from the age of 8 years who have had an inadequate response to (or are unable to take) phototherapies or other systemic therapies.

2. BEFORE YOU USE ENBREL

Do not use Enbrel

- **Allergy:** Do not use Enbrel if you, or the child you are caring for, are allergic to etanercept or any of the other ingredients of Enbrel. If you or the child experience allergic reactions such as chest tightness, wheezing, dizziness or rash, do not inject more Enbrel, and contact your doctor immediately.
- **Serious blood infection:** Do not use Enbrel if you or the child have, or are at risk of developing a serious blood infection called sepsis. If you are not sure, please contact your doctor.
- **Infections:** Do not use Enbrel if you or the child have an infection of any kind. If you are not sure, please talk to your doctor.

Take special care with Enbrel

- **Allergic reactions:** If you or the child experience allergic reactions such as chest tightness, wheezing, dizziness or rash, do not inject more Enbrel, and contact your doctor immediately.
- **Infections/surgery:** If you or the child develop a new infection, or are about to have any major surgery, your doctor may wish to monitor the treatment with Enbrel.
- **Infections/diabetes:** Tell your doctor if you or the child 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 outside the European region. If you or the child develop 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.
- **Tuberculosis:** As cases of tuberculosis have been reported in patients treated with Enbrel, your doctor will check for signs and symptoms of tuberculosis before starting Enbrel. 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 Alert Card. It is very important that you tell your doctor if you or the child 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:** Your doctor may decide to test for the presence of hepatitis B infection before you or the child begin treatment with Enbrel.
- **Hepatitis C:** Tell your doctor if you or the child have hepatitis C. Your doctor may wish to monitor the treatment with Enbrel in case the infection worsens.
- **Blood disorders:** Seek medical advice immediately if you or the child 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.
- **Nervous system and eye disorders:** Tell your doctor if you or the child 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 is an appropriate treatment.
- **Congestive heart failure:** Tell your doctor if you or the child have a history of congestive heart failure, because Enbrel 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.
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 may have an increased risk of developing lymphoma or another cancer.

Some children and teenage patients who have received Enbrel or other medicines that work the same way as Enbrel have developed cancers, including unusual types, which sometimes resulted in death.

Some patients receiving Enbrel 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.

- **Vaccinations:** If possible, children should be up to date with all vaccinations before using Enbrel. Some vaccines, such as oral polio vaccine, should not be given while using Enbrel. Please consult your doctor before you or the child receive any vaccines.
- **Chickenpox:** Tell your doctor if you or the child are exposed to chickenpox when using Enbrel. Your doctor will determine if preventive treatment for chickenpox is appropriate.
- **Latex:** The needle cap of the MYCLIC pen is made from latex (dry natural rubber). Contact your doctor before using Enbrel if the needle cap will be handled by, or Enbrel will be given to, someone with a known or possible hypersensitivity (allergy) to latex.
- **Alcohol abuse:** Enbrel 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 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 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.
- **Inflammatory bowel disease (IBD):** There have been cases of IBD in patients with juvenile idiopathic arthritis (JIA) treated with Enbrel. Tell the doctor if the child develops any abdominal cramps and pain, diarrhoea, weight loss or blood in the stool.

Using other medicines

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

Taking Enbrel with food and drink

Enbrel can be taken with or without food or drink.

Pregnancy and breast-feeding

The effects of Enbrel in pregnant women are not known, and so the use of Enbrel during pregnancy is not recommended. Women using Enbrel should not become pregnant. If the patient becomes pregnant, you should consult the patient's doctor.

Women using Enbrel should not breast-feed, since it is not known if Enbrel passes into human breast milk.

Driving and using machines

The use of Enbrel is not expected to affect the ability to drive or use machines.

3. HOW TO USE ENBREL

Always use Enbrel exactly as your doctor has told you. You should check with your doctor if or pharmacist you are not sure.

If you feel that the effect of Enbrel is too strong or too weak, talk to your doctor or pharmacist.

You have been prescribed a 50 mg strength of Enbrel. A 25 mg strength of Enbrel is available for doses of 25 mg.

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.

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 and whether retreatment is needed based on your response. If Enbrel has no effect on your condition after 12 weeks, your doctor may tell you to stop taking this medicine.

Dosing for children and adolescents

The appropriate dose and frequency of dosing for the child or adolescent will depend on body weight and disease. Patients weighing less than 62.5 kg should use Enbrel 25 mg/ml powder and solvent for solution for injection for paediatric use (see below for dosing for specific indications. Patients weighing 62.5 kg or more may use a fixed-dose pre-filled syringe or pre-filled pen.

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

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

Method and route of administration

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

Enbrel can be taken with or without food or drink.

Detailed instructions on how to inject Enbrel are provided in section 7, "USING THE MYCLIC PRE-FILLED PEN TO INJECT ENBREL". Do not mix the Enbrel 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 should be used.

If you use more Enbrel than you should

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

If you forget to inject Enbrel

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

Your symptoms may return upon discontinuation.

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

4. POSSIBLE SIDE EFFECTS

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

Other side effects that are not listed in this leaflet may occur. If you are concerned about any side effect, or if you notice any side effects that are not listed in this leaflet, please tell your doctor or pharmacist.

Allergic reactions

If any of the following happen, do not inject more Enbrel. 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, 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 **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

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 frequency of possible side effects listed below is defined using the following convention:

- Very common (affects more than 1 user in 10)
- Common (affects 1 to 10 users in 100)
- Uncommon (affects 1 to 10 users in 1,000)
- Rare (affects 1 to 10 users in 10,000)
- Very rare (affects less than 1 user in 10,000)
- Not known (frequency cannot be estimated from the available data)

The side effects listed below are those that have been seen in adult patients. The side effects seen in children and adolescents are similar to those seen in adults.

- **Very common:** Infections (including colds, sinusitis, bronchitis, urinary tract infections and skin infections); injection site reactions (including bleeding, bruising, redness, itching, pain, and swelling). Reactions at the injection site are very common, but do not occur as often after the first month of treatment. Some patients have developed a reaction at an injection site that was used before.
- **Common:** allergic reactions; fever; itching; antibodies directed against normal tissue (autoantibody formation).
- **Uncommon:** serious infections (including pneumonia, deep skin infections, joint infections, blood infection, and infections at various sites); 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); rash; inflammation or scarring of the lungs.
- **Rare:** serious allergic reactions (including severe localised swelling of the skin and wheezing); lymphoma (a type of blood cancer); 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; worsening congestive heart failure; seizures; lupus or lupus-like syndrome (symptoms may include persistent rash, fever, joint pain, and tiredness); inflammation of the blood vessels; low red blood cell count, low white blood cell count, low neutrophil (a type of white blood cell) count; elevated liver blood tests; skin rash, which may lead to severe blistering and peeling of the skin.
- **Very rare:** failure of the bone marrow to produce crucial blood cells.

- **Not known:** leukaemia (cancer affecting the blood and bone marrow); Merkel cell carcinoma (a type of skin cancer); excessive activation of white blood cells associated with inflammation (macrophage activation syndrome).

5. HOW TO STORE ENBREL

Keep out of the reach and sight of children.

Do not use Enbrel after the expiry date which is stated on the carton and on the MYCLIC pre-filled pen after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2° – 8°C). Do not freeze.

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

After taking a pre-filled pen from the refrigerator, **wait approximately 15-30 minutes to allow the Enbrel solution in the pen to reach room temperature.** Do not warm in any other way. Immediate use is then recommended.

Inspect the solution in the pen by looking through the clear inspection window. Only inject the solution in the pen if it is clear, colourless or pale yellow, and free from easily visible particles. If it is not, use a different syringe, then contact your pharmacist for assistance.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Enbrel contains

The active substance in Enbrel is etanercept. Each MYCLIC pre-filled pen contains 50 mg of etanercept.

The other ingredients are sucrose, sodium chloride, L-arginine hydrochloride, sodium phosphate monobasic dihydrate and sodium phosphate dibasic dihydrate, and water for injections.

What Enbrel looks like and contents of the pack

Enbrel is supplied as a solution for injection in a pre-filled pen (MYCLIC) (solution for injection). The MYCLIC pen contains a clear, colourless or pale yellow solution for injection. Each pack contains 2, 4 or 12 pens and 4, 8 or 24 alcohol swabs). Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

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This leaflet was last approved in

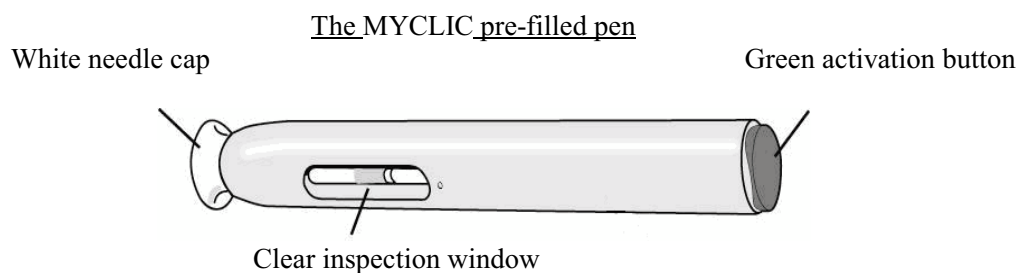
Detailed information on this product is available on the website of the European Medicines Agency
<http://www.ema.europa.eu>

7. USING THE MYCLIC PRE-FILLED PEN TO INJECT ENBREL

This section is divided into the following subsections:

Introduction**Step 1: Preparing for an Enbrel injection****Step 2: Choosing an injection site****Step 3: Injecting the Enbrel solution****Step 4: Disposing of the used MYCLIC pen****Introduction**

The instructions below explain how to use the MYCLIC pen to inject Enbrel. Please read the instructions carefully, and follow them step by step. Your doctor or nurse will tell you how to inject Enbrel. Do not attempt to administer an injection until you are sure that you understand how to use the MYCLIC pen properly. If you have questions about how to inject, please ask your doctor or nurse for help.

Diagram 1**Step 1: Preparing for an Enbrel injection**

1. Select a clean, well-lit, flat surface.
2. Gather the items that you will need for your injection, and place them on the chosen surface:

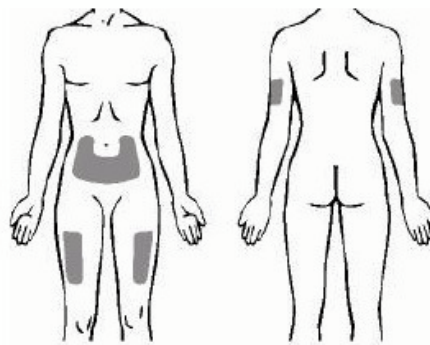
- a. **One MYCLIC pre-filled pen and one alcohol swab** (take these from the carton of pens you keep in your refrigerator). Do not shake the pen.
 - b. **One cotton ball or gauze**
3. Inspect the solution in the pen by looking through the clear inspection window. Only inject the solution in the pen if it is clear, colourless or pale yellow, and free from easily visible particles. If it is not, use a different syringe, then contact your pharmacist for assistance.
4. Leave the white needle cap in place and wait approximately 15-30 minutes to allow the Enbrel solution in the pen to reach room temperature. Waiting until the solution reaches room temperature may make the injection more comfortable for you. Do not warm in any other way. **Always leave the pen out of sight and reach of children.**

Whilst waiting for the solution in the pen to reach room temperature, read Step 2 (below), and choose an injection site.

Step 2: Choosing an injection site (see diagram 2)

1. The recommended injection site is the middle of the front of the thighs. If you prefer, you may alternatively use the stomach area, but make sure you choose a site at least 5 cm away from the belly button (navel). If someone else is giving you the injection, the outer area of the upper arms may also be used.

Diagram 2

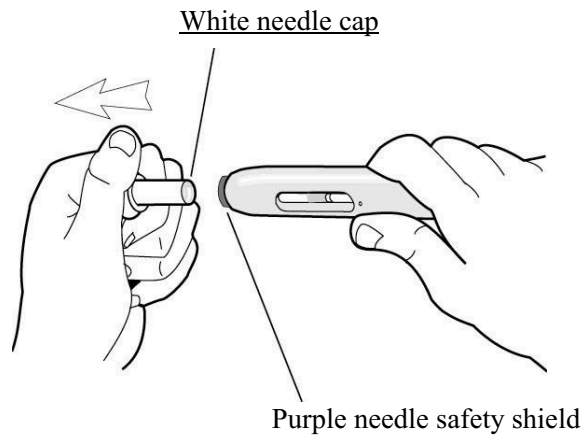


2. Each injection should be given at least 3 cm from where you last injected. Do not inject into tender, bruised or hard skin. Avoid scars or stretch marks. (It may be helpful to keep notes on the location of the previous injections.)
3. If you have psoriasis, you should try not to inject directly into any raised, thick, red, or scaly skin.

Step 3: Injecting the Enbrel solution

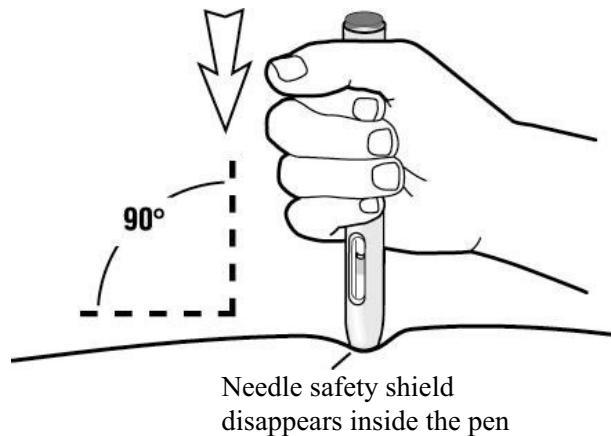
1. After waiting approximately 15-30 minutes for the solution in the pen to warm to room temperature, wash your hands with soap and water.
2. Clean the injection site with the alcohol swab using a circular motion, and allow it to dry. Do not touch this area again before injecting.
3. Pick up the pen, and remove the white needle cap by pulling it straight off (see Diagram 3). To avoid damaging the needle inside the pen, do not bend the white needle cap while you are removing it, and do not re-attach it once it has been removed. After removal of the needle cap, you will see a purple needle safety shield extending slightly from the end of the pen. The needle will remain protected inside the pen until the pen is activated.

Diagram 3



4. Lightly pinching the skin between the thumb and index finger of your free hand may make the injection easier and more comfortable.
5. **Without pressing the green activation button on top of the pen**, hold the pen at a right angle (90°) to the injection site, and press the open end of the pen firmly against the skin, so that the needle safety shield is pushed completely inside of the pen. A slight depression in the skin will be seen (see Diagram 4). Note that the green activation button will remain locked, and the pen will not activate, unless the needle shield is completely pushed inside the pen.

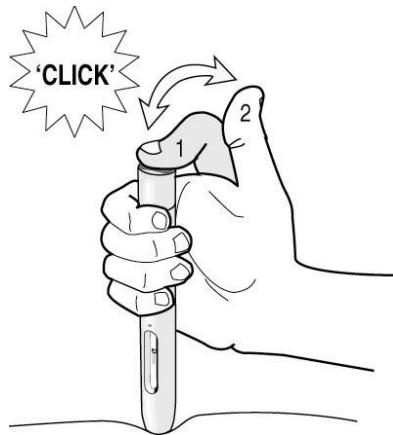
Diagram 4



6. Whilst pushing the pen firmly against the skin to ensure that the needle safety shield is fully depressed inside the pen, press **and immediately release** the green button on top of the pen with your thumb to start the injection (see Diagram 5). On pressing the button, you will hear a click. **Continue to hold the pen firmly against your skin until you hear a second click**, or until 10 seconds after the first click (whichever happens first).

Note – Remember to remove your thumb from the button once you hear the first click, or else there will be no second click when the injection is complete. You do not need to keep your thumb on the button in order to inject Enbrel.

Diagram 5



7. On hearing the second 'click' (or, if you do not hear a second 'click', after 10 seconds have passed), your injection will be complete (see diagram 6). You may now lift the pen from your skin (see diagram 7). As you lift the pen, the purple needle safety shield will automatically extend to cover the needle.

Diagram 6

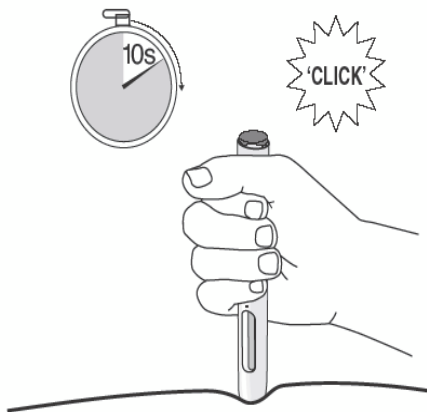
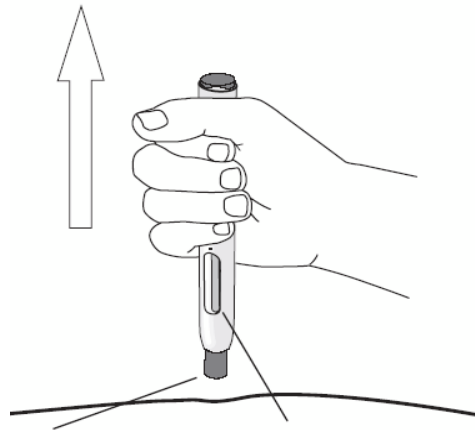


Diagram 7



Purple needle safety shield
extends to cover needle

Inspection window will
have turned purple

8. The pen's inspection window should now be completely purple, confirming that the dose has been injected correctly. If the window is not completely purple, contact your nurse or pharmacist for assistance, since the pen may not have injected the Enbrel solution completely. Do not try to use the pen again, and do not try to use another pen without agreement from your nurse or pharmacist.
9. If you notice a spot of blood at the injection site, you should press the cotton ball or gauze over the injection site for 10 seconds. Do not rub the injection site.

Step 4: Disposing of the used MYCLIC pen

- The pen should be used once only - it should never be re-used. Dispose of the used pen as instructed by your doctor, nurse or pharmacist.

If you have any questions, please talk to a doctor, nurse or pharmacist who is familiar with Enbrel.