EPREX® PREFILLED SYRINGE

Epoetin alfa (2000IU/0.5ml, 4000IU/0.4ml, 10 000IU/ml, 40 000IU/ml)

What is in this leaflet

What EPREX® is used for

EPREX® is used to treat symptomatic anemia caused by kidney disease
- in children on hemodialysis
- in adults on hemodialysis, peritoneal dialysis or not yet undergoing dialysis.

If you have kidney disease, you may be short of red blood cells if your kidney does not produce enough erythropoietin (necessary for red cell production). EPREX® is prescribed to stimulate your bone marrow to produce more red blood cells.

EPREX® is used to treat anemia if you are receiving chemotherapy for solid tumors, malignant lymphoma or multiple myeloma (bone marrow cancer) and your doctor decides you may have a need for a blood transfusion. EPREX® can reduce the need for a blood transfusion.

EPREX® is used in moderately anemic people who donate some of their blood before surgery, so that it can be given back to them during or after the operation. Because EPREX® stimulates the production of red blood cells, doctors can take more blood from these people.

EPREX® is used in moderately anemic adults about to have major surgery (bone), to reduce the potential need for blood transfusions.

EPREX® is used to treat anemia if you are an adult receiving a medicine called zidovudine (AZT) used to treat HIV infection.

How EPREX® works

EPREX® contains the active substance epoetin alfa - a protein that stimulates the bone marrow to produce more red blood cells which carry hemoglobin (a substance that transports oxygen). Epoetin alfa is a copy of the human protein erythropoietin (ee-rith-roe-po-eh-tin) and acts in the same way.

Before you use EPREX®

- *When you must not use it*

  Do not use EPREX®:
  - If you have high blood pressure not properly controlled with medicines.
  - Seizures
  - If you are allergic (hypersensitive) to Epoetin alfa or any of the other ingredients of EPREX® (see Product description – Inactive ingredients)
  - If you are due to have major orthopedic surgery (such as hip or knee surgery), and you:
    - have severe heart disease
    - have severe disorders of the veins and arteries
    - have recently had a heart attack or stroke
    - can't take medicines to thin the blood. EPREX® may not be suitable for you. Please discuss with your doctor. While on EPREX®, some people need medicines to reduce the risk of blood clots. If you can't take medicines that prevent blood clotting, you must not have EPREX®.
  - If you have been diagnosed with Pure Red Cell Aplasia (the bone marrow cannot produce enough red blood cells) after previous treatment with any product that stimulates red blood cell production (including EPREX®). See Side Effects.
  - To stimulate the production of your red blood cells (so that doctors can take more blood from you) if you cannot have transfusions with your own blood during or after surgery.

  EPREX® should not be used:
  - after the expiry date on the label and outer carton
  - if you know, or think that it may have been accidentally frozen, or
  - if there has been a refrigerator failure.

- *Before you start to use it*

  Take special care with EPREX®.

  EPREX® and other products that stimulate red cell production may increase the risk of developing blood clots in all patients. This risk may be higher if you have other risk factors for developing blood clots (for example, if you have had a blood clot in the past or are overweight, have diabetes, have heart disease or you are off your feet for a long time because of surgery or illness). Please tell your doctor about any of these things. Your doctor will help you to decide if EPREX® is suitable for you.

  It is important to tell your doctor if any of the following apply to you. You may still be able to use EPREX®, but discuss it with your doctor first.

  - If you know you suffer, or have suffered, from:
    - high blood pressure
    - epileptic seizures or fits
    - liver disease
    - anemia from other causes
    - porphyria (a rare blood disorder)

  - If you are a cancer patient, be aware that products that stimulate red blood cell production (like EPREX®) may act as a growth factor and therefore in theory may affect the progression of your cancer. Depending on your individual situation a blood transfusion may be preferable. Please discuss this with your doctor.

  - If you are a cancer patient, be aware that use of EPREX® may be associated with shorter survival and a higher death rate in head and neck, and metastatic breast cancer patients who are receiving chemotherapy.

  - If you experience a severe skin reaction, a rash, which may be severe, may cover your whole body and can also include blisters or areas of skin coming off, stop using EPREX® and call your doctor or get medical help right away.

Pregnancy, breast-feeding and fertility
It is important to tell your doctor if any of the following apply to you. You may still be able to use EPREX®, but discuss it with your doctor first.
- If you are pregnant, planning to become pregnant, or think you may be pregnant.
- If you are breast feeding, or are planning to breast-feed.

- *Taking other medicines*
EPREX® does not normally react with other medicines but please tell your doctor if you are using (or have recently used) any other medicines – including medicines obtained without a prescription.

If you are taking a drug called cyclosporin (used e.g. after kidney transplants), your doctor may order blood tests to check the level of cyclosporin while you are taking EPREX®.

Iron supplements and other blood stimulants may increase the effectiveness of EPREX®. Your doctor will decide if it is right for you to take them.

If you visit a hospital, clinic or family doctor, tell them you are having EPREX® treatment. It may affect other treatments or test results.

If you are a patient with hepatitis C and you receive interferon and ribavirin: You should discuss this with your doctor because a combination of epoetin alfa with interferon and ribavirin has led to a loss of effect and development of a condition called pure red cell aplasia (PRCA), a severe form of anemia, in rare cases. EPREX® is not approved in the management of anemia associated with hepatitis C.

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

How to use EPREX®
Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Your doctor has carried out blood tests and decided you need EPREX®.

EPREX® may be given by injection:
- Either into a vein or a tube that goes into a vein (intravenously)
  - EPREX® should be administered over at least one to five minutes, depending on the total dose.
- Or under the skin (subcutaneously).

Your doctor will decide how EPREX® will be injected. Usually the injections will be given to you by a doctor, nurse or other healthcare professional. Some people, depending on why they need EPREX® treatment, may later learn how to inject themselves under the skin: see Instructions on how to inject EPREX® yourself.

Instructions on how to inject EPREX® yourself
How to inject yourself using a pre-filled syringe:

When treatment starts, EPREX® is usually injected by medical or nursing staff. Later, your doctor may suggest that you or your caregiver learn how to inject EPREX® under the skin (subcutaneously) yourself.

- Do not attempt to inject yourself unless you have been trained to do so by your doctor or nurse.
- Always use EPREX® exactly as instructed by your doctor or nurse.
- Only use EPREX® if it has been stored correctly – see Storage and disposal of EPREX®
- Before use, leave the EPREX® syringe to stand until it reaches room temperature. This usually takes between 15 and 30 minutes.

Only take one dose of EPREX® from each syringe. If any liquid remains in the syringe after an injection, the syringe should be properly disposed of, not reused.

If EPREX® is injected under the skin (subcutaneously), the amount injected is not normally more than one milliliter (1 mL) in a single injection. The injections should be given in the arms, legs or the stomach area.

EPREX® is given alone and not mixed with other liquids for injection.

Do not shake EPREX® syringes. Prolonged vigorous shaking may damage the product. If the product has been shaken vigorously, don't use it.

The pre-filled syringes are fitted with the PROTECS™ needle guard device to help prevent needle stick injuries after use. This is indicated on the packaging.

Figure 1 shows what the pre-filled syringes looks like.

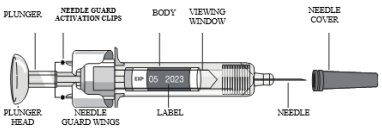

Figure 1

- Take a syringe out of the refrigerator. The liquid needs to come to room temperature. Do not remove the syringe's needle cover while allowing it to reach room temperature.
- Check the syringe, to make sure it is the right dose, has not passed its expiry date, is not damaged, and the liquid is clear and not frozen.
- Choose an injection site. Good sites are the top of the thigh and around the tummy (abdomen) but away from the navel. Vary the site from day to day.
- Wash your hands. Use an antiseptic swab on the injection site, to disinfect it.
- Hold the pre-filled syringe by the body of the syringe with the covered needle pointing upward.
- Do not hold by the plunger head, plunger, needle guard wings, or needle cover.
- Do not pull back on the plunger at any time.
- Do not remove the needle cover from the pre-filled syringe until you are ready to inject your EPREX®.
- Take the cover off the syringe by holding the barrel and pulling the cover off carefully without twisting it. Don't push the plunger, touch the needle or shake the syringe.
- Countries with prefilled syringes fitted with the PROTECS™ needle guard device include this sentence: Do not touch the needle activation clips (as indicated by asterisks* in Figure 1) to prevent prematurely covering the needle with the needle guard.
- Pinch a fold of skin between your thumb and index finger. Don't squeeze it.
- Push the needle in fully. Your doctor or nurse may have shown you how to do this.
- Push the plunger with your thumb as far as it will go to inject the entire amount of liquid. Push it slowly and evenly, keeping the skin fold pinched. Countries with prefilled syringes fitted with the PROTECS™ needle guard device

include this sentence: The PROTECS™ needle guard will not activate unless the entire dose is given. You may hear a click when the PROTECS™ needle guard has been activated.
- When the plunger is pushed as far as it will go, take out the needle and let go of the skin.
- Slowly take your thumb off the plunger. Countries with prefilled syringes fitted with the PROTECS™ needle guard device include this sentence: Allow the syringe to move up until the entire needle is covered by the PROTECS™ needle guard.
- When the needle is pulled out of your skin, there may be a little bleeding at the injection site. This is normal. You can press an antiseptic swab over the injection site for a few seconds after the injection.
- Dispose of your used syringe in a safe container – see section 5, How to store EPREX®.

- *How much to use*
The dose of EPREX® you receive is based on your bodyweight in kilograms. The cause of your anemia is also a factor in your doctor deciding the correct dose.

Your doctor will monitor your blood pressure regularly while you are using EPREX®.

- *When to use it*
Use as directed by your doctor or pharmacist.

- *How long to use it*
Continue taking EPREX® for as long as your doctor recommends.

- *If you forget to use it*
Make the next injection as soon as you remember. If you are within a day of your next injection, forget the missed one and carry on with your normal schedule. Do not double up the injections.

- *If you use too much (overdose)*
Tell the doctor or nurse immediately if you think too much EPREX® has been injected. Side effects from an overdose of EPREX® are unlikely.

While you are using EPREX®
- *Things you must do*
Always follow your doctor's instructions carefully.

- *Things you must not do*
  - Do not use EPREX® to treat any other complaint unless your doctor says so.
  - Do not give this medicine to anyone else, even if their symptoms seem similar to yours.

- *Things to be careful of*
Take special care with other products that stimulate red blood cell production:

EPREX® is one of a group of products that stimulate the production of red blood cells like the human protein erythropoietin does. Your healthcare professional will always record the exact product you are using.

If you are given a product in this group other than EPREX® during your treatment, speak to your doctor or pharmacist before using it.

Side Effects
Like all medicines, EPREX® can cause side effects, although not everybody gets them.

Tell your doctor or nurse immediately if you notice any of the effects in this list.

The most frequently occurring adverse reactions observed in clinical trials of epoetin alfa were:
- High blood pressure
- Diarrhea
- Nausea
- Vomiting
- Fever
- Headache
- Flu-like symptoms: more common at the start of treatment.

Very rare side effects include:
- Erythropoetin antibody-mediated pure red cell aplasia
- Thrombocythemia (increased of platelet cells in blood)

Tell your doctor or nurse immediately if you are aware of any of these effects, or if you notice any other effects while you are receiving treatment with EPREX®.

You may report any side effects or adverse drug reactions directly to the National Centre for Adverse Drug Reaction Monitoring by calling Tel: 03-7883 5549, or visiting the website npra.moh.gov.my (Public → Reporting Side Effects to Medicines (ConSERF or Vaccines (AEFI)).

Storage and disposal of EPREX®
- *Storage*
Keep this medicine out of the sight and reach of children.
Do not use this medicine after the expiry date, which is stated on the box and on the label after the letters EXP. The expiry date refers to the last day of that month.

Store in a refrigerator 2°C-8°C (36°F to 46°F). You may take EPREX® out of the refrigerator and keep it at room temperature (up to 25°C) for no longer than 7 days. Once a syringe has been removed from the refrigerator and has reached room temperature (up to 25°C) it must either be used within 7 days or disposed of.
Do not freeze or shake.

Store in the original package in order to protect from light.

Do not use this medicine if you notice that the seal is broken or if the liquid is colored or you can see particles floating in it. In the event of either being observed, discard the medicinal product.

- *Disposal*
Do not throw away any medicines via waste water or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

Product description
- *What it looks like*
EPREX® is presented as a solution for injection in a pre-filled syringe. The pre-filled syringes are fitted with the PROTECS™ needle guard device. EPREX® is a clear, colorless solution.

EPREX® is supplied in type I glass prefilled syringes with FluroTec®-coated rubber stoppers.

- *Ingredients*
  - *Active ingredient*
    Epoetin alfa

  - *Inactive ingredients*
    disodium phosphate dihydrate;
    glycine and water for injections;
    polysorbate 80, sodium chloride, and
    sodium dihydrogen phosphate
    dihydrate.

- *MAL number(s)*
  2000IU/0.5ml
  MAL19962530AZ

  4000IU/0.4ml
  MAL19962532AZ

  10000IU/ml
  MAL19962533AZ

  40000IU/ml
  MAL20034248AZ

Manufacturer
Cilag AG,
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Product registration holder
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