PACKAGE LEAFLET: INFORMATION FOR THE USER

EPREX 2,000 IU/ml, 4,000 IU/ml AND 10,000 IU/ml SOLUTION FOR INJECTION in PRE-FILLED SYRINGES
(epoetin alfa)

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse 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 any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist.

In this leaflet:

1. What EPREX is and what it is used for
2. Before you use EPREX
3. How to use EPREX
4. Possible side effects
5. How to store EPREX
6. Further information

1. WHAT EPREX IS AND WHAT IT IS USED FOR

EPREX contains epoetin alfa - a protein that stimulates the bone marrow to produce more red blood cells which carry haemoglobin (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.

- **EPREX is used to treat symptomatic anaemia caused by kidney disease**
  - in children on haemodialysis
  - in adults on haemodialysis or peritoneal dialysis
  - in severely anaemic adults 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 anaemia if you are receiving chemotherapy** for solid tumours, malignant lymphoma or multiple myeloma (bone marrow cancer) and your doctor decides you may have a high need for a blood transfusion. EPREX can reduce the need for a blood transfusion.

- **EPREX is used in moderately anaemic 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 can be used in moderately anaemic adults about to have major orthopaedic surgery** (*for example hip or knee replacement operations*), to reduce the need for potential blood transfusions.

2. BEFORE YOU USE EPREX

Do not use EPREX

- **If you have high blood pressure** not properly controlled with medicines.

- **If you are allergic (hypersensitive)** to epoetin alfa or any of the other ingredients of EPREX (listed in Section 6, *Further information*).

- **If you are due to have major orthopaedic 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 Section 4, *Possible 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.

Take special care with EPREX

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:
  - **heart disease, including *angina***;
  - **high blood pressure**;
  - **blood clots**, or you are at a higher risk for developing blood clots, (for example if you are overweight, have diabetes or you are off your feet for a long time because of surgery or illness).
  - **epileptic seizures** or fits
  - **anaemia from other causes**
  - **liver disease**
  - **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.**

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.

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 ciclosporin (used e.g. after kidney transplants), your doctor may order blood tests to check the level of ciclosporin 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.

Pregnancy and breast feeding

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, or think you may be pregnant.
- If you are breast feeding.

3. HOW TO USE EPREX

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)
- **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 health care 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.*

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.

The dose of EPREX you receive is based on your bodyweight in kilograms. The cause of your anaemia is also a factor in your doctor deciding the correct dose.

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

People with kidney disease

- Your doctor will maintain your haemoglobin level between 10 and 12 g/dl as a high haemoglobin level may increase the risk of blood clots and death.
- **The usual starting dose** of EPREX for adults and children is 50 International Units (IU) per kilogram (/kg) of bodyweight given three times a week. For patients on peritoneal dialysis EPREX is given twice a week.
- For adults and children EPREX is given as an injection either into a vein or a tube that goes into a vein. When this access (via a vein or tube) is not readily available, your Doctor may decide that EPREX should be injected under the skin (subcutaneously). This includes patients on peritoneal dialysis.

- Your doctor will order regular blood tests to see how your anaemia is responding and may adjust the dose, usually every four weeks.
- Once your anaemia has been corrected, your doctor will continue to check your blood regularly. Your EPREX dose and frequency of administration may be further adjusted to maintain your response to treatment.
- If you are on a more extended dosing interval (greater than once weekly) of EPREX, you may not maintain adequate haemoglobin levels and you may require an increase in EPREX dose or frequency of administration.
- You may be given iron supplements before and during EPREX treatment to make it more effective.
- If you are having dialysis treatment when you begin treatment with EPREX, your dialysis regime may need to be adjusted. Your doctor will decide this.

Adults on chemotherapy

- Your doctor may initiate treatment with EPREX if your haemoglobin is 10g/dl or less.
- Your doctor will maintain your haemoglobin level between 10 and 12 g/dl as a high haemoglobin level may increase the risk of blood clots and death.
- The starting dose is **either** 150 IU per kilogram bodyweight three times a week **or** 450 IU per kilogram bodyweight once a week.
- EPREX is given by injection under the skin.
- Your doctor will order blood tests, and may adjust the dose, depending on how your anaemia responds to EPREX treatment.
- You may be given iron supplements before and during EPREX treatment to make it more effective.
- You will usually continue EPREX treatment for one month after the end of chemotherapy.

Adults donating their own blood

- **The usual dose** is 600 IU per kilogram bodyweight twice a week.
- EPREX is given by injection into a vein, for 3 weeks before your surgery, after you have donated blood.
- You may be given iron supplements before and during EPREX treatment to make it more effective.

Adults scheduled for major orthopaedic surgery

- **The recommended dose** is 600 IU per kilogram bodyweight once a week.
- EPREX is given by injection under the skin for three weeks before surgery and on the day of surgery.
- If there is a medical need to reduce the time before your operation, you will be given a daily dose of 300 IU/kg for up to ten days before surgery, on the day of surgery and for four days immediately afterwards.
- If blood tests show your haemoglobin is too high before the operation, the treatment will be stopped.
- You may be given iron supplements before and during EPREX treatment to make it more effective.

Instructions on how to inject EPREX yourself

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.**
- **Ensure that you only inject the amount of liquid as instructed by your doctor or nurse.**
- **Only use EPREX if it has been stored correctly – see Section 5, *How to Store EPREX*.**
- **Before use, leave the EPREX syringe to stand until it reaches room temperature. This usually takes between 15 and 30 minutes. Use the syringe within 3 days of taking it out of the refrigerator.**

Only take one dose of EPREX from each syringe.

If EPREX is injected under the skin (subcutaneously), the amount injected is not normally more than one millilitre (1 ml) in a single injection.

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.

How to inject yourself using a pre-filled syringe:

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

- **Take a syringe out of the refrigerator.** The liquid needs to come to 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.
- **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.
- **Push the plunger to remove any unwanted liquid from the syringe before you inject under the skin** in order to only keep the amount of liquid as instructed by your doctor or nurse.
- **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.
- **Check that you haven't punctured a blood vessel.** Pull back slightly on the plunger. If you see blood, take the syringe out and try somewhere else.
- **Push the plunger with your thumb as far as it will go to inject the entire amount of liquid** corresponding to the correct dose to be injected. Push it slowly and evenly, keeping the skin fold pinched. **The needle safety device will not activate unless the entire dose is given.**
- **When the plunger is pushed as far as it will go**, take out the needle and let go of the skin.
- **Take your thumb off the plunger** and allow the syringe to move up until the entire needle is covered by the needle safety device.
- **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.*

If you use more EPREX than you should

Tell the doctor or nurse immediately if you think too much EPREX has been injected. Side effects from an overdose of EPREX are unlikely.

If you forget to use EPREX

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

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 lead 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 anaemia associated with hepatitis C.

4. POSSIBLE 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.

Very common side effects
These may affect more than 1 in every 10 people using EPREX.

- **Flu-like symptoms**, such as headache, aches and pains in the joints, feeling of weakness, tiredness and dizziness. These may be more common at the start of treatment. If you have these symptoms during intravenous injection, a slower delivery of the injection may help to avoid them in future.

- **Respiratory tract congestion**, such as stuffy nose and sore throat, has been reported in patients with kidney disease not yet on dialysis.

Common side effects
These may affect less than 10 in every 100 people using EPREX.

- **Increased blood pressure** in people with cancer and in people with symptomatic anaemia caused by kidney disease. **Headaches**, particularly sudden, stabbing migraine-like headaches, **feeling confused or having fits** may be signs of a sudden increase in blood pressure. This requires urgent treatment . Raised blood pressure may require treatment with drugs (or adjustment to any drugs you already take for high blood pressure).

- **Chest pain, breathlessness, painful swelling in the leg** which may be symptoms of blood clots (thrombosis).

- **Skin rashes and swelling around the eyes** (oedema), which may result from an allergic reaction.

If you are receiving haemodialysis:
- **Blood clots** (thrombosis) may form in your dialysis shunt. This is more likely if you have low blood pressure or if your fistula has complications.

- **Blood clots** may also form in your haemodialysis system. Your doctor may decide to increase your heparin dose during dialysis.

Very rare side effects
These may affect less than 1 in 10,000 people using EPREX.

- **Symptoms of pure red cell aplasia (PRCA)**

  PRCA means the inability to produce enough red blood cells in the bone marrow. PRCA can result in **sudden and severe anaemia. The symptoms are:**
  - **unusual tiredness,**
  - **feeling dizzy,**
  - **breathlessness**.

  PRCA has been very rarely reported after months to years of treatment with EPREX and other products that stimulate red blood cell production in patients with chronic renal failure.

If you are receiving haemodialysis an increase in levels of small blood cells (called platelets), which are normally involved in the formation of a blood clot may occur, particularly when starting treatment. Your doctor will check on this.

You may experience **redness, burning and pain at the site of injection**.

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**.**

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist.

5. HOW TO STORE EPREX

Keep out of the reach and sight of children.

Do not use EPREX 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). You may take EPREX out of the refrigerator and keep it at room temperature (up to 25°C) for no longer than 3 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 3 days or disposed of.

Do not freeze or shake.

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

Do not use EPREX if you notice that the seal is broken or if the liquid is coloured or you can see particles floating in it.

Don't use the EPREX syringes if any of these applies. Talk to a doctor or pharmacist.

Medicines should not be disposed of via waste water or in 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 EPREX contains:

The active substance is: Epoetin alfa (for quantity see the table below).
The other ingredients are: Polysorbate 80, sodium chloride, sodium dihydrogen phosphate dihydrate, disodium phosphate dihydrate, glycine and water for injections.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose i.e. essentially "sodium free".

What EPREX looks like and contents of the pack

EPREX is presented as a solution for injection in pre-filled syringes. The pre-filled syringes are fitted with a needle safety device (see the table below). Pack sizes of 6. EPREX is a clear, colourless solution.

Presentation	Corresponding Presentations in Quantity/Volume for each Strength	Amount of epoetin alfa
Pre-filled syringes with needle safety device	2000 IU/ml: 1,000 IU/0.5 ml	 8.4 micrograms
	4000 IU/ml: 2,000 IU/0.5 ml	 16.8 micrograms
	10,000 IU/ml: 3,000 IU/0.3 ml 4,000 IU/0.4 ml 5,000 IU/0.5 ml 6,000 IU/0.6 ml 8,000 IU/0.8 ml 10,000 IU/1 ml	 25.2 micrograms 33.6 micrograms 42.0 micrograms 50.4 micrograms 67.2 micrograms 84.0 micrograms

Not all packs may be marketed.

Marketing Authorisation Holder

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This medicinal product is authorised in the Member States of the EEA under the following names:

Austria: ERYPO®
Belgium: EPREX®
Germany: ERYPO®
Denmark: EPREX®
Greece: EPREX®
Finland: EPREX®
France: EPREX®
Ireland: EPREX®
Italy: EPREX®
Luxemburg: EPREX®
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