PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

Schedule 4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM

EPREX® range

Recombinant human erythropoietin (r-HuEPO)

Pre-filled syringes (Solution for injection):

EPREX® 2 000 IU/0,5 mL

EPREX® 4 000 IU/0,4 mL

EPREX® 6 000 IU/0,6 mL

EPREX® 10 000 IU/1,0 mL

EPREX® 40 000 IU/1,0 mL

Read all of this leaflet carefully before you are given EPREX

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- EPREX 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.

1. WHAT EPREX CONTAINS

- The active ingredient is recombinant human erythropoietin (r-HuEPO).

PRE-FILLED SYRINGE COMPONENTS	**CONCENTRATION PER PRE-FILLED SYRINGE**

Active ingredient r-HuEPO	2 000 IU/0,5 mL	4 000 IU/0,4 mL	6 000 IU/0,6 mL	10 000 IU/1,0 mL	40 000 IU/1,0 mL
	16,8 µg/0,5 mL	33,6 µg/0,4 mL	50,4 µg/0,6 mL	84 µg/1,0 mL	336 µg/1,0 mL

- The other ingredients are: disodium phosphate dihydrate, glycine, polysorbate 80, sodium chloride, sodium dihydrogen phosphate dihydrate and water for injection.
- Contains no preservatives.

2. WHAT EXPREX IS USED FOR

EPREX is a solution for injection, which 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 and acts in the same way.

- EPREX is used to treat symptomatic anaemia caused by kidney disease.
- EPREX is also used to treat anaemia if you are receiving chemotherapy for some cancers.
- 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.

3. BEFORE YOU ARE GIVEN EPREX

You should not be given EPREX:

- **if you have been diagnosed with antibody-mediated pure red cell aplasia (PRCA**) [i.e. 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 *POSSIBLE SIDE EFFECTS*.
- **if you have high blood pressure**, which is not properly controlled.
- **If you are hypersensitive (allergic)** to animal derived products.
- **If you are hypersensitive (allergic)** to the active substance (erythropoeitin) or any of the other ingredients of EPREX. (Refer to *WHAT EPREX CONTAINS*, above).
- **If you are a cancer patient** be aware that EPREX may act as a growth factor and therefore may affect the progression of your cancer. Please discuss this with your doctor.
- **If for any reason you cannot receive medicines to thin blood**. If you can't take medicines that prevent blood clotting, you must not have EPREX.
- **If you are due to have major surgery** and have not predonated your own blood and have severe heart disease or disorders of the veins and arteries or have had a recent heart attack or stroke.
- **To stimulate the production of your red blood cells** (so that the 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:

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 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 fits or seizures,
    - liver disease,
    - anaemia 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 the use of EPREX may be associated with shorter survival and 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.

<u>Take special care with other products that stimulate red blood cell production:</u>

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 first before using it.

Pregnancy and Breastfeeding:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or healthcare professional for advice before using EPREX.

There are no adequate and well-controlled studies in pregnant women.

Driving and using machinery:

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

Taking other medicines with EPREX:

Always tell your healthcare professional if you are taking any other medicine. (This includes complementary or traditional medicines.)

If you are taking a medicine called ciclosporin to suppress your immune system, your doctor may order special blood tests to measure ciclosporin levels while you are using 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.

4. HOW TO USE EPREX

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

Always use EPREX exactly as your doctor has instructed you. You should check with your doctor of pharmacist if you are unsure.

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 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.

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 accidently frozen, or
- if there has been a refrigerator failure.

The dose of EPREX you receive is based on your body weight 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 in adults, as a high haemoglobin level may increase the risk of blood clots and death.
- The usual starting dose of EPREX for adults is 50 International Units (IU) per kilogram (/kg) of bodyweight given three times a week.
- For peritoneal dialysis patients, EPREX may be given twice a week for adults.
- For adult haemodialysis patients, EPREX may be given three times a week.
- For adults 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 dialysis and patients not yet on dialysis.

- Your doctor will order regular blood tests to see how your anaemia is responding and may adjust the dose, usually no more frequently than 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.
- 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 10 g/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/kg bodyweight three times a week or 40 000 IU subcutaneously 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/kg bodyweight twice a week for three weeks.
- 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 orthopedic surgery

- The recommended dose is 600 IU/kg 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

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*) for 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 section *STORING AND DISPOSING 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 and 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.

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 syringe looks like.

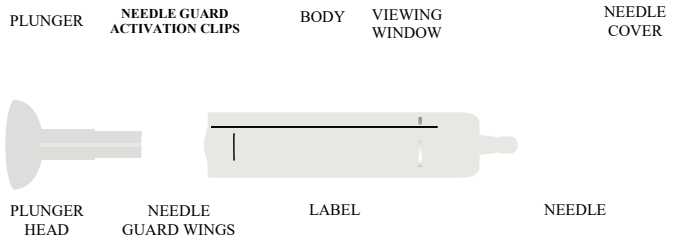


Figure 1

- **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.
- **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. **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**. 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 *STORING AND DISPOSING OF EPREX.*

If you receive 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.

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

If you forget to use EPREX:

Inject 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 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 anaemia, in rare cases. EPREX is not approved in the management of anaemia associated with hepatitis C.

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

5. POSSIBLE SIDE EFFECTS

EPREX can cause side effects. Not all side effects reported for EPREX are included in ths leaflet. Should your general health worsen, or if you experience any untoward effects while using EPREX, please consult your doctor, pharmacist or other healthcare professional for advice.

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

Frequent side effects:

- Diarrhoea,
- Feeling sick in your stomach,
- Vomiting,
- Fever,
- Increased blood pressure. 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 medicines (or adjustment to any medicines you already take for high blood pressure),
- Blood clots (including deep vein thrombosis and embolism) that may require urgent treatment. You may have chest pain, breathlessness, and painful swelling and redness, usually in the leg as symptoms,
- Blocked blood vessel by a blood clot,
- Blood clots including those that: move to lungs, cause chest pain and shortness of breath; blocks blood supply to the eye, which may cause blurred vision or blindness; block an artery; cause a heart attack; stroke, or temporary block blood flow to part of the brain (mini-stroke),
- Cough,
- Skin rashes, which may be the result from an allergic reaction,
- Bone, muscle or joint pain,
- Flu-like symptoms, such as headaches, aches and pains in the joints, feeling of weakness, chills, tiredness and dizziness. These may be more common at the start of treatment. If you have these symptoms during injection into the vein, a slower delivery of the injection may help to avoid them in the future,
- Redness, burning and pain at the site of injection,
- Swelling of the ankles, feet or fingers,

- Arm or leg pain.

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.

Less frequent side effects

- High levels of blood potassium which can cause abnormal heart rhythm (this is a very common side effect in patients on dialysis),
- Fits,
- Nose or airway congestion,
- Allergic reaction,
- Hives,
- **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.
- 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.

- Severe allergic reaction that may include:
    - A swollen face, lips, mouth, tongue or throat,
    - Difficulty in swallowing or breathing,
    - Itchy rash (hives).
- Problem with the blood that may cause pain, dark coloured urine or increased sensitivity of the skin to sunlight (porphyria),
- Medicine ineffective,
- An uncommon disorder in which your body produces too many blood platelets. This condition may cause you to feel fatigued, lightheaded and to experience headaches and vision changes. It also increases your risk of blood clots (thrombocythanaemia).

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

6. STORING AND DISPOSING OF EPREX

Store all medicines out of reach of children.

Store EPREX in the original package (to protect it from light) in a refrigerator between 2 and 8 ^{0}C. Do not freeze or shake EPREX.

EPREX can be kept for only a limited period. EPREX pre-filled syringes that are being used or about to be used can be kept at room temperature (not above 25 °C) for a maximum single period of 3 days.

Do not use EPREX:

- after the date (month and year) mentioned after “EXP”, even if it has been stored properly;
- if the seal is broken;
- if the liquid is coloured or you can see particles floating in it;
- if you know, or think that it may have been accidentally frozen; or

- if there has been a refrigerator failure.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets)

7. PRESENTATION OF EPREX

EPREX pre-filled syringes are 1 mL colourless glass syringes with fixed needles for single-dose use. Six pre-filled syringes are supplied in a carton. The pre-filled syringes are fitted with the PROTECS™ needle guard device to help prevent needle stick injuries after use.

8. IDENTIFICATION OF EPREX

A clear, colourless solution, free from visible foreign particles.

9. REGISTRATION NUMBERS

Pre-filled syringes

EPREX 2000/0,5 mL	29/8.3/0769
EPREX 4000/0,4 mL	29/8.3/0770
EPREX 6000/0,6 mL	35/8.3/0415
EPREX 10 000/ 1,0 mL	W/8.3/221
EPREX 40 000/1,0 mL	35/8.3/0036

10. THE NAME, BUSINESS ADDRESS AND TELEPHONE NUMBER OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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11. DATE OF PUBLICATION

- Date of registration of the EPREX pre-filled syringe range:
    - EPREX 2 000 IU/0,5 mL: 26 June 1995
    - EPREX 4 000 IU/0,4 mL: 26 June 1995
    - EPREX 6 000 IU/0,6 mL: 20 September 2002
    - EPREX 10 000 IU/1,0 mL: 30 October 1991
    - EPREX 40 000 IU/1,0 mL: 10 August 2002
- Date of the most recently revised Patient Information Leaflet as approved by the Advisory Clinical Committee: 02 June 2021