

Package leaflet: Information for the user

EPREX 2,000 IU/mL, 4,000 IU/mL, 10,000 IU/mL AND 40,000 IU/mL solution for injection in pre-filled syringe (epoetin alfa)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- 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 only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, nurse, or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

1. What EPREX is and what it is used for ?

Pharmaco-therapeutic group: other ANTIANEMIC PREPARATIONS/ERYTHROPOIETIN – ATC code : B03XA01.

EPREX contains the active substance 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 in adults receiving chemotherapy for solid tumours, malignant lymphoma or multiple myeloma (bone marrow cancer) who may have a need for a blood transfusion. EPREX can reduce the need for a blood transfusion in these patients.

. EPREX is used in moderately anaemic adults 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 anaemic adults about to have major orthopaedic surgery** (for example hip or knee replacement operations), to reduce the potential need for blood transfusions.
- **EPREX is used to treat anaemia in adults with a bone marrow disorder that causes a severe disruption in the creation of blood cells (myelodysplastic syndromes).** EPREX can reduce the need for a blood transfusion.

2. What you need to know before you use EPREX ?

Do not use EPREX

- **If you are allergic** to epoetin alfa or any of the other ingredients of this medicine (listed in section 6).
- **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*.
- **If you have high blood pressure** not properly controlled with medicines.
- 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.
- **If you are due to have major elective 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.**

Warnings and precautions

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**
 - **anaemia from other causes**
 - **porphyria (a rare blood disorder)**
 - **an allergy to latex. The needle cover of this medicinal product contains latex rubber which may cause severe allergic reactions in people who are sensitive to latex. See section 4 for the signs of an allergic reaction.**

- **If you are a patient with chronic renal failure**, and particularly if you do not respond properly to EPREX, your doctor will check your dose of EPREX because repeatedly increasing your dose of EPREX if you are not responding to treatment may increase the risk of having a problem of the heart or the blood vessels and could increase risk of myocardial infarction, stroke and death.

- **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.

- Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with epoetin treatment.

SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications.

If you develop a serious rash or another of these skin symptoms, stop taking EPREX and contact your doctor or seek medical attention immediately.

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.

Children and adolescents

Not applicable.

Other medicines and EPREX

Tell your doctor if you are taking, have recently taken or might take any other medicines.

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.

Eporex with food, drinks and alcohol

Not applicable.

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.**

Driving and using machines

Not applicable.

EPREX contains sodium

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially “sodium free.”

3. 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)
- . **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. In children the haemoglobin level should be maintained between 9.5 and 11 g/dL.
- **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 may be 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 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. A rise in haemoglobin of greater than 2 g/dL over a four week period should be avoided.
- 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. Your doctor will use the lowest effective dose to control the symptoms of your anaemia.
- If you do not respond adequately to EPREX, your doctor will check your dose and will inform you if you need to change doses of EPREX.
- 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 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 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 immediately after you have donated blood for 3 weeks before your surgery.
- . 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 each week 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.

Adults with myelodysplastic syndrome

- . Your doctor may initiate treatment with EPREX if your haemoglobin is 10 g/dL or less. The aim of treatment is to maintain your haemoglobin level between 10 and 12 g/dL as a higher haemoglobin level may increase the risk of blood clots and death.
- . EPREX is given by injection under the skin.
- . The starting dose is 450 IU per kilogram bodyweight once a week.
- . Your doctor will order blood tests, and may adjust the dose, depending on how your anaemia responds to EPREX treatment.

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.**
- . **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.**

Only take one dose of EPREX from each syringe .

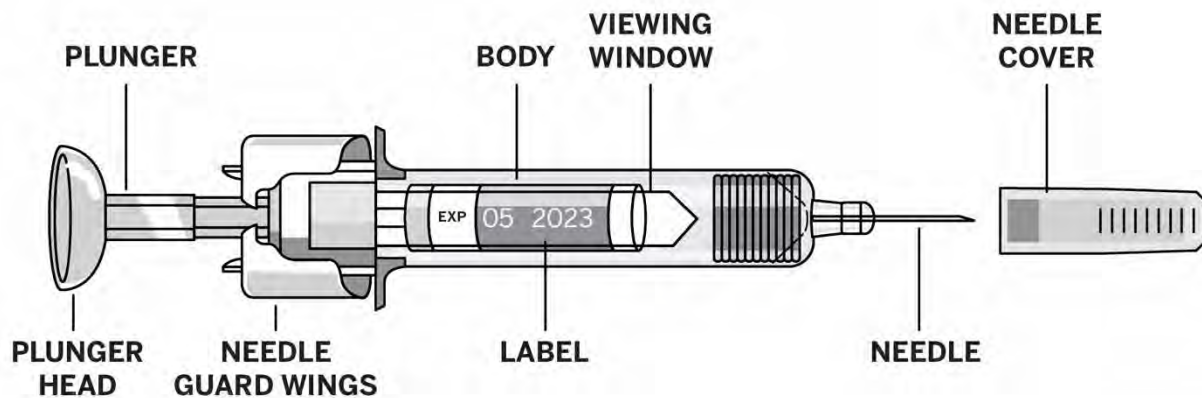
If EPREX is injected under the skin (subcutaneously), the amount injected is not normally more than one millilitre (1 mL) in a single injection.

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 subcutaneously using a pre-filled syringe:

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.



- **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.
- **Remove the plunger from the label from the syringe. If you cannot see the numbered graduations through the viewing window, hold the body of the syringe and gently turn the syringe by the needle cover to line up the numbered graduations to the viewing window.**
- **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 needle cover off the syringe** by holding the body and pulling the needle cover off carefully without twisting it. Don't touch the needle or shake the syringe.
- **Remove the air bubble by holding the syringe with the needle pointing up and gently pressing the plunger until a drop of liquid comes out of the needle tip.**
- **In case you only need a partial dose of the syringe as indicated by your doctor, push the plunger until the desired numbered graduation mark to remove unwanted liquid before injection.**
- **Do not touch the needle guard wings 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** to 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.

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 to make up for a forgotten dose.

If you stop using EPREX

Not applicable.

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.

4. Possible side effects

Like all medicines, this medicine 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.

Serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis have been reported in association with epoetin treatment. These can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms. Stop using EPREX if you develop these symptoms and contact your doctor or seek medical attention immediately. See also section 2.

Very common side effects

These may affect more than 1 in 10 people treated by EPREX.

- . **Diarrhoea**
- . **Feeling sick in your stomach**
- . **Vomiting**
- . **Fever**
- . **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 up to 1 in 10 people treated by EPREX.

- . **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 drugs (or adjustment to any drugs 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.
- . **Cough.**
- . **Skin rashes, which may result from an allergic reaction.**
- . **Bone or muscle pain.**
- . **Flu-like symptoms**, such as headache, 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.**

Uncommon side effects

These may affect up to 1 in 100 people treated by EPREX.

- . **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**

Rare side effects

These may affect up to 1 in 1,000 people treated by EPREX.

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

PRCA means the bone marrow does not make enough red blood cells. PRCA causes **sudden and severe anaemia**. The symptoms are:

- . **unusual tiredness,**
- . **feeling dizzy,**
- . **breathlessness.**

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

- . 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:
 - o **a swollen face, lips, mouth, tongue or throat,**
 - o **difficulty swallowing or breathing,**
 - o **itchy rash (hives).**
- . Problem with the blood that may cause pain, dark coloured urine or increased sensitivity of the skin to sunlight (porphyria).

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.

Reporting of side effects

If you get any side effects, talk to your doctor, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store EPREX ?

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). 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 this medicine if you notice that the seal is broken or if the liquid is coloured or you can see particles floating in it. In the event of either being observed, discard the medicinal product.

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.

6. Contents of the pack and other 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.

What EPREX looks like and contents of the pack

EPREX is presented as a solution for injection in pre-filled syringe. The pre-filled syringes are fitted with the PROTECS™ needle guard device (see the table below). EPREX is a clear, colourless solution.

| Presentation* | Corresponding Presentations in Quantity/Volume for each Strength | Amount of epoetin alfa |
|---|---|------------------------------------|
| Packs of 6 single pre-filled syringes with PROTECS™ needle guard device | <u>2,000 IU/mL:</u> 1,000 IU/0.5 mL | 8.4 micrograms |
| | <u>4,000 IU/mL:</u> 2,000 IU/0.5 mL | 16.8 micrograms |
| | <u>10,000 IU/mL:</u> 4,000 IU/0.4 mL | 33.6 micrograms |
| | 6,000 IU/0.6 mL 10,000 IU/1 mL | 50.4 micrograms 84.0 micrograms |
| Packs of 1 single pre-filled syringe with PROTECS™ needle guard device | 40,000 IU/1 mL | 336 micrograms |

*Not all packs may be marketed.

MAH:

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Manufacturer:

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To contact us, go to www.janssen.com/contact-us

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THIS IS A MEDICAMENT

- Medicament is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament. The doctor and the pharmacist are the experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of the reach of children

Council of Arab Health Ministers, Union of Arab Pharmacists