

PART III: CONSUMER INFORMATION

PrEPREX®
epoetin alfa

Sterile Solution

This leaflet is Part III of a three-part "Product Monograph" published when EPREX® was approved for sale in Canada and is designed specifically for Consumers. Please read this carefully before you start to take your medicine. This leaflet is a summary and will not tell you everything about EPREX®. Contact your doctor or pharmacist if you have any questions about the drug.

INFORMATION ABOUT ANEMIA**What is anemia:**

Anemia is a condition where your blood contains a lower than normal number of red blood cells. Red blood cells contain a substance called hemoglobin that is responsible for transporting oxygen in your blood. As the number of red blood cells in your blood decreases, so does the amount of oxygen delivered to your body. Development of anemia is characterized by several symptoms, such as weakness, fatigue, shortness of breath, dizziness, poor concentration and chills. These symptoms over time can negatively impact your overall quality of life.

What causes anemia:

Anemia may be the result of several causes, including blood loss or nutritional deficiencies. Anemia due to blood loss must be investigated and treated by a physician. Nutritional anemia caused by a deficiency of iron, vitamin B₁₂ or folic acid can be treated with dietary supplements. Anemia can also be caused by chronic disease, such as cancer or kidney (renal) disease.

Anemia in Chronic Kidney Disease:

In chronic kidney disease, anemia results when the kidneys are unable to manufacture enough natural erythropoietin to stimulate the bone marrow to produce more red blood cells.

Anemia in Cancer:

Anemia in cancer can be caused by the chemotherapy regimens used to treat the cancer. The toxic effects of chemotherapy reduce the body's ability to produce erythropoietin as well as the bone marrow's ability to respond and make more red blood cells. As a result, not enough red blood cells are produced and the patient becomes anemic.

ABOUT THIS MEDICATION**What the medication is used for:**

EPREX® is used to increase the production of red blood cells and to decrease the need for red blood cell transfusion. The dose should be gradually adjusted to achieve this goal. EPREX® may be used in adults and children with chronic kidney disease; adults who have HIV-infection and are receiving a drug called zidovudine; adult cancer patients receiving chemotherapy; and adults scheduled to undergo major elective surgery.

What it does:

EPREX® is a protein made in the laboratory which acts like a substance naturally made in the human body called erythropoietin. Erythropoietin controls the production of red blood cells in the body.

When it should not be used:

You should not use EPREX® if:

- you are allergic to any of the ingredients in the product;
- 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 **Serious Warnings and Precautions**;
- you have uncontrolled high blood pressure;
- 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;
- while on EPREX®, some people may need medicines to reduce the risk of blood clots. You should not take EPREX® if you cannot for any reason take medicines that prevent blood clotting.

What the medicinal ingredient is:

epoetin alfa

What the nonmedicinal ingredients are:

Glycine and polysorbate 80 as stabilizers, sodium chloride, water for injection and sodium phosphate

Pre-filled syringes do not contain preservatives.

The needle cover of the pre-filled syringe contains dry natural rubber (a derivative of latex), which should not be handled by persons sensitive to this substance.

What dosage forms it comes in:

Single-use pre-filled syringes with PROTECS® needle guard: 1,000 IU/0.5 mL, 2,000 IU/0.5 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/mL, 20,000 IU/0.5 mL, 30,000 IU/0.75 mL, 40,000 IU/mL

To reduce the risk of accidental needle sticks to users, each pre-filled syringe is equipped with the PROTECS® needle guard that is automatically activated to cover the needle after complete delivery of the syringe content.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

ALL PATIENTS

- To minimize the risks for death and serious cardiovascular (heart and blood vessel-related) side effects, your doctor will follow the recommended dosage for each indication.
- Patients with uncontrolled hypertension should not be treated with EPREX®; blood pressure should be controlled adequately before initiation of therapy.
- EPREX® should be used with caution in patients with a history of seizures.
- During hemodialysis, patients treated with EPREX® may require increased anticoagulation with heparin to prevent clotting of the artificial kidney. Patients with pre-existing vascular disease should be monitored closely.
- Hemoglobin levels during EPREX® treatment should not be higher than 120 g/L (may not apply to surgery patients).
- If you undergo surgery while taking EPREX®, your physician may prescribe a blood thinner, as appropriate for the surgical procedure, to prevent blood clots.
- Antibody-mediated pure red cell aplasia (PRCA) has been reported after treatment with recombinant erythropoietins. If you develop PRCA, you may suddenly become severely anemic and this could result in a dependency on blood transfusions.

CHRONIC RENAL FAILURE PATIENTS

- If your hemoglobin is kept too high, you have an increased chance of heart attack, stroke, heart failure, blood clots and death. Your doctor will try to keep your hemoglobin between 100 and 115 g/L, not exceeding 120 g/L.

CANCER PATIENTS

- If you are a cancer patient and your hemoglobin is kept too high (over 120 g/L),
 - your tumor may grow faster,
 - you have an increased chance of heart attack, stroke, blood clots and death.
- Your doctor should use the lowest dose of EPREX® needed to avoid red blood cell transfusions.
- In some instances, red blood cell transfusion should be the preferred treatment option.
- Once you have finished your chemotherapy course, EPREX® should be discontinued.

BEFORE taking EPREX®:

- Tell your doctor about any medical problems and about any allergies you have or have had in the past.
- Tell your doctor if you have or have had high blood pressure, seizures, blood clots, liver disease, porphyria (a rare blood disorder), or gout.
- While you are treated with EPREX® your doctor will need to check your blood pressure. Your blood pressure will be monitored carefully and any changes outside of the guidelines that your doctor has given you must be reported. If your blood pressure increases, you may need medication to lower it. If you already take blood pressure medication, your doctor may increase the amount.
- Your doctor will also measure your serum iron levels, red blood cell levels and other factors in your blood, prior to starting and during treatment with EPREX®, as deemed appropriate.
- If you are on dialysis, your dialysis prescription may need to be changed while you are being treated with EPREX®. Your doctor will take blood tests to determine if any change is needed. Your doctor may also need to adjust any medication you receive to prevent blood clotting.
- Tell your doctor if you are pregnant, if you think you might be pregnant, or if you are trying to become pregnant.
- Tell your doctor if you are breast-feeding.
- In many women with severe kidney failure, the monthly period may stop. When these women take EPREX® they may restart their monthly cycle. If you are a woman with kidney disease, you should discuss contraception with your doctor.
- In patients with kidney disease, due to the possibility of an increase in blood pressure, there is a small chance of having a seizure when therapy starts. During the initial phase of treatment, your doctor may advise you to avoid driving, using machines or doing anything else that could be dangerous if you are not alert.
- If you are a home dialysis patient, you should continue to check your access, as your doctor or nurse has shown you, to make sure it is working. Be sure to let your healthcare professional know right away if there is a problem.
- If you are a cancer patient you should be aware that EPREX® is a red blood cell growth factor and in some circumstances your cancer may grow faster. You should discuss treatment options for your anemia with your doctor.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor about all medications you are using, including those obtained without a prescription and any other remedies or dietary supplements. It is especially important that your doctor know if you are taking high blood pressure medication.

PROPER USE OF THIS MEDICATION

EPREX[®] may be given by injection:

Either into a vein or a tube that goes into a vein (intravenously) by healthcare professional
Or under the skin (subcutaneously) into the arms, legs or abdomen

While you are receiving EPREX[®], your doctor will measure your red blood cells. Your doctor will use this information to adjust the dose to the amount right for you.

Follow your doctor's instructions about when and how to take this medication.

Do not shake EPREX[®] Sterile Solution. The solution in pre-filled syringe should always be clear and colourless. Do not use EPREX[®] Sterile Solution if the contents of the pre-filled syringe appear discoloured or cloudy, or if pre-filled syringe appears to contain lumps, flakes, or particles. If the pre-filled syringe has been shaken vigorously, the solution may appear to be frothy and should not be used.

Pre-filled syringes of EPREX[®] Sterile Solution do not contain preservatives and therefore are to be used once and discarded. Any unused portion of a pre-filled syringe should not be used.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

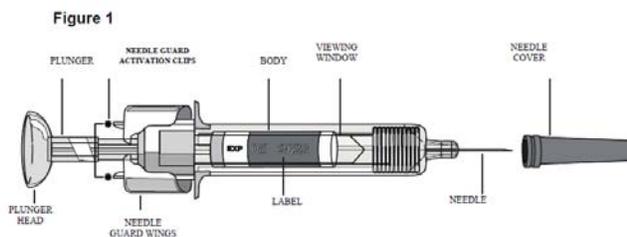
Missed Dose:

If you miss a dose, contact your doctor for instructions.

Subcutaneous Injection: Preparing and Injecting the Dose

Important: To help avoid contamination and possible infection, follow these instructions exactly.

Single-Use Pre-filled Syringe with PROTECS[®] needle guard



To reduce the risk of accidental needle sticks to users, each pre-filled syringe is equipped with the PROTECS[®] needle

guard that is automatically activated to cover the needle after complete delivery of the syringe content.

1. **Take a syringe out of the refrigerator.** The liquid needs to come to room temperature. This usually takes between 15 to 30 minutes. Do not remove the syringe's needle cover while allowing it to reach room temperature.
2. **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.

3. **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.



4. **Wash your hands. Use an antiseptic swab on the injection site,** to disinfect it.
5. **Hold the pre-filled syringe by the body of the syringe with the covered needle pointing upward.**
6. **Do not hold by the plunger head, plunger, needle guard wings, or needle cover.**
7. **Do not pull back on the plunger at any time.**
8. **Do not remove the needle cover from the pre-filled syringe until you are ready to inject your EPREX[®].**
9. **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.
10. **Do not touch the needle activation clips (as indicated by asterisks * in Figure 1, to prevent prematurely covering the needle with the needle guard.**

11. **Pinch a fold of skin** between your thumb and index finger. Don't squeeze it.

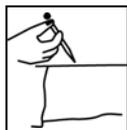


12. **Push the needle in fully.** Your doctor or nurse may have shown you how to do this.



13. **Push the plunger with your thumb as far as it will go to inject all of the liquid.** Push it slowly and evenly, keeping the skinfold 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.**

14. **When the plunger is pushed as far as it will go**, take out the needle and let go of the skin.



15. **Slowly take your thumb off the plunger.** Allow the syringe to move up until the entire needle is covered by the needle guard.
16. **When the needle is pulled out of your skin, there may be a little bleeding at the injection site. This is normal. Press an antiseptic swab** over the injection site for a few seconds after the injection.
17. **Dispose of your used syringe** in a safe container (see **Disposal of Syringes**).
18. **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 (see **Disposal of Syringes**).

Disposal of Syringes

1. Place all used needles and syringes in a hard plastic container with a screw-on cap, or a metal container with a plastic lid, such as a coffee can properly labelled as to content. If a metal container is used, cut a small hole in the plastic lid and tape the lid to the metal container. If a hard-plastic container is used, always screw the cap on tightly after each use. When the container is full, tape around the cap or lid, and dispose of according to your doctor's instructions.
2. Do not use glass or clear plastic containers (or any other container) that will be recycled or returned to a store.
3. Always store the container out of the reach of children.
4. Please check with your doctor, nurse, or pharmacist for other suggestions.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Any medicine may have unwanted effects. The side effects you might experience may vary depending on the reason you are taking EPREX®. Tell your doctor or pharmacist about any unusual sign or symptom whether listed or not. The side effects reported most often in all patients receiving EPREX® are high blood pressure and flu-like symptoms such as dizziness, drowsiness, fever, headache, muscle and joint pain and weakness, and gastrointestinal disturbances such as nausea, vomiting and diarrhea. Redness, burning and pain at the place where EPREX® is given have also been reported.

Call your doctor right away if you have an increase in headaches or develop unusual headaches, such as sudden stabbing migraine like headache as this may be a sign of very high blood pressure.

There is a possible association of a worsening of increased blood pressure if red blood cell production occurs too rapidly. Your doctor may need to reduce your dose of EPREX® and initiate or increase blood pressure medication. Signs and symptoms of serious cardiovascular events may include but are not limited to: chest pain, leg pain and swelling, shortness of breath, sudden weakness, numbing or tingling of face, arm or leg, an increase in headaches or severe sudden headaches, loss of vision or loss of speech, lightheadedness.

Patients experiencing these signs or symptoms should contact their doctor immediately.

Patients should NOT discontinue their medication without consulting their doctor first.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Additional side effects which have been reported more often in chronic renal failure patients than other patients include increases in blood pressure, clotted access, seizures and pure red cell aplasia (PRCA). PRCA is a condition in which severe and sudden anemia (characterized by symptoms such as severe tiredness/fatigue, and shortness of breath on mild exertion) develops due to failure of the bone marrow to produce red blood cells. PRCA could result in a dependency on blood transfusions. Should you be diagnosed with PRCA, your doctor will stop your EPREX® therapy and may initiate treatment with drugs and/or blood transfusions to help increase your red blood cell count.

If you develop signs of allergy such as difficulty breathing, hives, itching, rash, or swelling of the throat, face, eyelids, mouth or tongue, discontinue the use of EPREX® and contact your doctor or obtain medical help immediately.

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.

This is not a complete list of side effects. For any unexpected effects while taking EPREX®, contact your doctor or pharmacist.

HOW TO STORE IT

- Store unopened in a refrigerator between 2 and 8 degrees centigrade. Do not freeze. Protect from light.
- Do not use this product after the expiry date written on the package.

- Keep this and all medicines in a safe place away from children.
- If you are using EPREX[®] at home, it is important that the syringe be stored in your refrigerator although not in the freezer compartment. EPREX[®] should not be frozen. Do not use EPREX[®] if it has been frozen. Leave the EPREX[®] syringe to stand for about 15 to 30 minutes until it reaches room temperature prior to using it.
- When the pre-filled syringe is about to be used, it may be removed from the refrigerator and stored at room temperature (not above 25°C) for one single period of maximum 7 days.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 1908C
Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect[®] Canada Web site at www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting

***NOTE:** Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.*

MORE INFORMATION

For questions, concerns, or the full Product Monograph go to: www.janssen.com/canada or contact the manufacturer, Janssen Inc., at: 1-800-567-3331 or 1-800-387-8781.

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