EPOTIN

Recombinant Human Erythropoietin
Vials

Epotin, a recombinant human erythropoietin type-α, is a glycoprotein hormone which stimulates the division and differentiation of committed erythroid progenitors in the bone marrow.
Epotin has the same biological and immunological effects as endogenous erythropoietin and contains the identical amino acid sequence of isolated neutral erythropoietin.

Composition
Each vial contains:
Active ingredient: Recombinant human erythropoietin 1,000 Units, 2,000 Units, or 4,000 Units.
(Host: CHO cell, Vector: SV40)
Stabilizer: Human serum albumin 2.5mg/mL.

Description
Epotin is a sterile, colorless solution in glass containers (vials).

Indications
– ***Treatment of Anaemia of Chronic Renal Failure Patients***
Epotin is indicated in the treatment of anaemia associated with chronic renal failure, including patients on dialysis and patients not on dialysis. **Epotin** is indicated to elevate or maintain the red blood cell level and to decrease the need for transfusions.
– ***Treatment of Anaemia in Cancer Patients on Chemotherapy***
Epotin is indicated to elevate the red blood cell level to donate autologous blood. **Epotin** is also indicated to prevent from reduction of haemoglobin for the patients scheduled to major surgery who are not able to participate in an autologous blood donation program as in the following conditions:
1. Patients with low haemoglobin concentration.
2. Patients scheduled to major surgery, female needs more than 4 units of blood or male needs more than 5 units of blood.
3. In case of short time before surgery to donate autologous blood.

Dosage and administration
– ***Chronic Renal Failure (CRF) Patients***
Epotin is administered intravenously at an initial dose of 50 units/kg for 1-2 minutes three times a week. It can be given by either an intravenous or subcutaneous route for patients with CRF not on dialysis. The dose increase is dependent upon the initial response. The dose can be increased, if necessary, by 25 units/kg in 4-week period. If haemoglobin is increased more than 2g/dl at a dose of 50 units/kg, the frequency should be reduced to two times a week. To correct the anaemia, the target concentration of haemoglobin is 10g/dl (30% as haematocrit). When the anaemia is corrected, **Epotin** is given as a maintenance dose of 25-50 units/kg two or three times a week. The target range of haemoglobin is 10-12g/dl. The patients with pretreatment haemoglobin < 6g/dl need higher maintenance dose than the patients with pretreatment haemoglobin > 8g/dl. And the dose may be adjusted according to the age of the patients. The unit dose of **Epotin** should not exceed 200 units/kg, and the frequency should not be more than three times a week. Prior to initiation of therapy or during the therapy, the patient's iron stores should be evaluated, if necessary, iron should be supplied. If the patients are in aluminum intoxication or infected, delayed or diminished responses may be occurred. In patients with CRF not on dialysis, the maintenance dose must also be individualized according to the severity of anaemia or age, however, the dose of 70-150 units/kg per week have been shown to maintain 36-38% of haematocrit for more than six months.
– ***Cancer patients on chemotherapy***
The recommended initial dose of **Epotin** is 150 units/kg as a subcutaneous injection three times a week. If the response is unsatisfactory after 8 weeks of therapy, the dose can be increased up to 300 units/kg three times a week. If patients have not responded satisfactorily to an **Epotin** dose of 300 units/kg three times a week, it is unlikely that they will respond to higher doses of **Epotin**. If the haematocrit exceeds 40%, the dose of **Epotin** should be withheld until it falls to 36%. The dose of **Epotin** should be reduced by 25% when treatment is resumed or the dose is titrated to maintain the desired haematocrit. If the initial dose of **Epotin** includes a very rapid haematocrit response (e.g., an increase of more than 4% points in any 2-week period), the dose should be reduced. In general, patients with lower baseline serum erythropoietin levels responded more vigorously to **Epotin** than patients with higher erythropoietin levels. Although no specific serum erythropoietin level can be stipulated above which patients would be unlikely to respond to **Epotin** therapy, treatment of patients with grossly elevated serum erythropoietin levels higher than 200mU/mL is not recommended. The haematocrit should be monitored on a weekly basis in patients receiving **Epotin** therapy until haematocrit becomes stable.
– ***Patients to be participated in autologous blood donation program***
Prior to major surgery, it is recommended to take autologous blood two times a week for 3 weeks. Based on previous studies, **Epotin** can be given intravenously at a dose of 150 - 300 units/kg, two times a week for 3 weeks to elevate the red blood cell levels. The recommended maximum dose to promote erythropoiesis is 600 units/kg, two times a week for 3 weeks intravenously. The concentration of haemoglobin should be controlled weekly for the patients who are expected to require > 4units of blood with pretreatment of haemoglobin > 11g/dl (Hb l < 6.8 mmol/L), the patients require > 5 units of blood with pretreatment haemoglobin > 11g/dl (Hb l < 6.8mmol/L), or the patients to be scheduled to surgery within 1-3 weeks. Iron supplementation: All surgery patients being treated with **Epotin** should receive adequate iron supplementation (e.g., 200mg of iron preparations per day, P.O) throughout the course of therapy in order to support erythropoiesis and avoid depletion of iron stores. Iron supplementation should be initiated as soon as possible, several weeks before taking blood.

Contraindications
Epotin is contraindicated in patients with:
– Known hypersensitivity to the drug or to other erythropoietin products.
– Uncontrolled hypertension.
– Known hypersensitivity to mammalian cell-derived products or Albumin (Human).

Precautions
Epotin should be administered with caution to following patients:
– Patients with hypertension (blood pressure may rise or hypertensive encephalopathy may occur during **Epotin** therapy).
– Patients with known history of a hypersensitivity to drugs.
– Patients with known history of allergic reactions to drugs.
– Patients with myocardial infarction, pulmonary infarction, or cerebral embolus.
– Patients with cerebral bleeding or premature infant with cerebral bleeding.

Side Effects
– Shock: As shock has been reported, full observation should be taken. If the symptoms appear, the administration should be discontinued and an appropriate treatment should be taken.

- Cardiovascular: Hypertension, thrombosis of lacrimal duct or A-V shunt, and tachycardia have been reported rarely.
- Hypertensive encephalopathy: As hypertensive encephalopathy (shows headache, conscious disorder and seizures) and cerebral haemorrhage have been reported occasionally, the drug should be administered cautiously with observation of the trends of blood pressure and haematocrit during the therapy.
- Cerebral embolus: As cerebral embolus has been reported, full observation should be taken. If the symptoms appear, the administration should be discontinued and an appropriate treatment should be taken.
- Skin: Itching, skin rash, and decubitus have been reported.
- Liver: Elevation in AST, ALT, LDH, ALP, and total bilirubin may occur occasionally.
- Gastrointestinal tract: Nausea, vomiting, anorexia, diarrhea, and abdominal pain may occur occasionally.
- Blood: Leukocytosis, eosinophilia have been reported occasionally. On occasion, granulocytopenia may be occurred in premature infant. Increased serum potassium, BUN, creatinine and uric acid have been reported occasionally.
- Others: Cerebral haemorrhage in the eyes, splenomegaly, nasal haemorrhage, oedema, headache, dizziness, fever, fatigue, arthralgia, myalgia, bitter taste in mouth, tremor and oedema of eyelid may be occasionally associated with **Epotin** therapy.
- Studies analyzed to date indicate that **Epotin** is generally well-tolerated. The adverse reactions reported are frequent sequelae from patient's disease, and are not necessarily attributable to **Epotin** therapy.

Warnings

- **Epotin** treatment should be limited in anaemic patients with CRF less than 10g/dl of haemoglobin (30% as haematocrit) or cancer patients with serum erythropoietin less than 200mU/mL.
- **Epotin** should not be used in patients with anaemia from blood loss, haematocytopenia, and aluminum intoxication.
- Special monitoring of patient's history should be done to forecast shock or other responses. Low dosage should be allowed by intravenous route to determine a patient's responsiveness to the administration of **Epotin** before initiating the therapy or resuming it after withholding.
- During the **Epotin** therapy, haemoglobin concentration or haematocrit should be observed periodically (once a week at initial therapy, biweekly at maintenance therapy). Special caution should be taken not to result in excessive erythropoiesis (more than 12g/dl of haemoglobin or 36% of haematocrit). In case of excessive erythropoiesis, withholding of the drug or appropriate treatment should be taken.
- Hypertension and hypertensive encephalopathy have been reported in patients treated with **Epotin**, associated with a significant increase in haematocrit. Haematocrit increase may occur in case of discontinuation of the therapy. Blood pressure in patients treated with **Epotin** should be monitored carefully, particularly in patients with an underlying history of hypertension or cardiovascular disease. The dosage should be adjusted in patients with a fast rate of rise of haematocrit (greater than 4% in any two-week period) owing to the potential for an increased risk.
- Seizures have occurred in patients with CRF. In patients on dialysis, there was a higher incidence of seizures during the first 90 days of therapy (occurring in approximately 2.5% of patients) as compared with later time points. Seizures also have occurred in cancer patients on chemotherapy.
- The thrombotic events may occur such as myocardial infarction, pulmonary embolism, cerebrovascular accident, or ischemic attack. The patients with vascular disease should be monitored cautiously.
- Since hyperkalaemia may occur, the importance of compliance with dietary prescriptions should be reinforced.
- Shunt infarct or residual blood in dialysis kit may also occur, so, carefully monitor the blood circulation in shunt or dialysis kit.
- In case of iron deficiency, adequate iron supplementation in order to support erythropoiesis should be done.
- **Epotin** is a growth factor that primarily stimulates red blood cell production. However, the possibility that **Epotin** can act as a growth factor for any tumor type, particularly myeloid malignancies, cannot be excluded.

Use in pregnant women: The safety of **Epotin** in pregnant women has not been established. **Epotin** should be used during pregnancy only if potential benefit justifies the potential risk.

Paediatric use: The safety of **Epotin** in children has not been established.

Geriatric use: When **Epotin** is administered to geriatric patients, dosage and frequency should be controlled on the basis of observed blood pressure, haemoglobin concentration or haematocrit.

Precautions in administration

- Do not dilute or administer in conjunction with other drug solutions.
- Administer **Epotin** after dialysis in patients on dialysis and slowly inject for longer than 5 minutes in patients with flu-like symptoms.
- **Epotin** should not be administered by intravenous infusion.

Overdosage

The dose response of **Epotin** depends upon the conditions of patient. In case of overdosage, hypertension may occur. If polycythaemia is of concern, phlebotomy may be indicated to decrease the haematocrit.

Presentation

Epotin vials: Pack of 10 vials.

* *Store at 2-8°C, protected from light.*

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 experts in medicines, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicaments out of the reach of the children.

Council of Arab Health Ministers,
Union of Arab Pharmacists.

Any information ? Call Our Toll Free No. **(971) 800-4994**

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Produced by: ***julphar***
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