

Only for the use of Medical Professionals

Recogen

Erythropoietin alfa

Description

Recogen® is the preparation of Erythropoietin Alfa which is a 165-amino aciderythropoiesis stimulating glycoprotein manufactured by recombinant DNA technology. Mechanism of action: **Recogen®** stimulates erythropoiesis by the same mechanism as endogenous erythropoietin.

Indication

Recogen is indicated for –

- The treatment of anemia due to chronic kidney disease (CKD), including patients on dialysis and not on dialysis to decrease the need for red blood cell (RBC) transfusion.
- Anemia associated with chronic renal failure in pediatric and adult patients on dialysis.
- The treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy.
- Adult patients with mild to moderate anemia ($100\text{g/L} < \text{hemoglobin level} < 130\text{g/L}$) scheduled for elective non cardiac, nonvascular surgery with an expected moderate blood loss (2-4 units or 900-1800) to reduce exposure to allogeneic blood transfusion and to facilitate erythropoietic recovery.
- The treatment of anemia due to zidovudine administered at $< 4200 \text{ mg/week}$ in HIV-infected patients with endogenous serum erythropoietin levels of $< 500 \text{ mUnits/ml}$.

Dosage and administration

Route of administration: **Recogen®** should be taken in intravenous or subcutaneous route. Do not shake and do not use **Recogen®** which has been shaken or frozen. Do not use any syringe exhibiting particulate matter or discoloration. Administer as intravenous injection over 1-2 minutes. Slow injection over 5 minutes may be beneficial to those who exhibit flu like symptoms. In patients on dialysis, the injection should follow dialysis procedure. Do not administer by IV infusion or in conjunction with other drug.

Chronic kidney disease

For all CKD patients

When initiating or adjusting therapy, monitoring of hemoglobin levels at least weekly until the level is stable, and then monitoring for at least monthly, is required. During adjustments, rate of increase and decrease of Hgb (hemoglobin) level, ESA (erythropoiesis stimulating agent) responsiveness and Hgb variability should be considered. In addition, following recommendation is to be considered:

- Dose should not be increased more frequently than once in every 4 weeks. Decreases in the dose can be done more frequently. Repeated dose alteration should be avoided. In case of rapid rise of Hgb (greater than 1 g/dL in any 2-week period), the dose should be reduced by 25% or more if required. In case of patients who are not responding to the treatment adequately (Hgb level less than 1 g/dL after 4 weeks of therapy), dose should be increased by 25%.
- For patients who don't respond after 12 weeks of treatment, increasing dose are unlikely to improve response and thus therapy should be discontinued. Evaluation of other causes of anemia is required.

For CKD patients on dialysis

- When the Hgb level is less than 10 g/dL, treatment should be initiated.
- If the Hgb level approaches or exceeds 11 g/dL, dose should be reduced or interrupted and the minimum dose of **Recogen®** should be used.
- Recommended starting dose for adult patient is 50-100 IU/kg 3 times per week by IV or SC route and starting dose for pediatric patient (1 month to 16 years) is 50 IU/kg weekly by IV (intravenous) or SC (subcutaneous) route. The IV route is recommended for patients on hemodialysis.

For CKD patients not on dialysis

- Initiation of **Recogen®** treatment should be considered only when the Hgb level is less than 10 g/dL and the following considerations apply:
- The rate of Hgb decline indicates the likelihood of requiring a RBC transfusion. Reducing the risks of alloimmunization and or other RBC transfusion-related risks is a goal.

If the Hgb level is greater than 10 g/dL, dose should be reduced or interrupted and the minimum dose of **Recogen®** should be used. Recommended starting dose for adult patient is 50-100 IU/kg 3 times weekly by IV or SC route.

Patients on cancer chemotherapy

- Therapy with **Recogen®** should only be initiated when the Hgb (Hemoglobin) is less than 10 g/dL and if there is a minimum of two additional months of planned chemotherapy.
- Recommended starting dose
The dose for adult patient is 150 IU/kg or 40000 IU per week by SC route until the completion of chemotherapy.

The dose for pediatric patient (5-18 years) is 600 IU/kg by IV route weekly until completion of chemotherapy.

Dose reduction

Dose should be reduced by 25% if:

- Hgb level is greater than 1 g/dL in any two week period
- Hgb level reaches a level needed to avoid RBC transfusion
- The dose should be withheld if Hgb exceeds a level needed to avoid RBC transfusion.

Dose increase

After the initial 4 weeks of therapy, if Hgb level increases by less than 1 g/dL or remains below 10 g/dL.

- The dose should be increased to 300 IU/kg 3 times a week or 60000 IU weekly in adult.
- 900 IU/kg weekly in children. The maximum dose for children in every week is 60000 IU.

After 8 weeks, if there is no response, **Recogen®** therapy should be discontinued.

HIV-infected patients treated with zidovudine

Starting dose

The recommended starting dose for adult is 100 IU/kg 3 times weekly by IV or SC route. The dose for pediatric patient (8 months -17 years) is 50-400 IU/kg 2-3 times a week by IV or SC route.

Dose adjustment

- If Hgb does not increase after 8 weeks of therapy, the dosage of **Recogen®** can be increased by 50 to 100 IU/kg at 4 to 8 weeks intervals until Hgb reaches a level needed to avoid RBC transfusion
- The dose should not exceed 300 IU/kg.

Therapy should be withheld if Hgb levels exceeds 12 g/dL and be resumed at a dose of 25% below the previous dose when Hgb is less than 11 g/dL. Therapy should be discontinued if an increase in Hgb is not achieved at doses of 300 IU/kg for 8 weeks.

Patient scheduled for surgery

Recommended **Recogen®** regimens are

- IU/kg/day by SC route for 10 days before surgery, on the day of surgery, and for 4 days after surgery.
- 600 IU/kg by SC route administered in 4 doses: 21, 14, and 7 days before surgery and on the day of surgery.

Concomitant patients on dialysis, the injection should follow the dialysis procedure. Prophylactic measurement for deep vein thrombosis is recommended during the therapy.

Geriatric use: No difference in safety and effectiveness were observed between elderly and younger patient.

Contraindication

Erythropoietin is contraindicated in patients with known hypersensitivity to erythropoietin or any components of this product. It is also contraindicated in patients with uncontrolled hypertension, known sensitivity to mammalian cell derived products, patients who develop pure red cell aplasia (PRCA) following treatment with any erythropoietin product should not receive erythropoietin alfa. The use of erythropoietin alfa is contraindicated in patients scheduled for cardiac and vascular surgery (and who are participating in an autologous blood pre-deposit program), in patients with severe coronary, peripheral arterial, carotid, or cerebral vascular disease, including patients with recent myocardial infarction or cerebral vascular accident.

Warning and precaution

Erythropoietin alfa should be used with caution in patients with history of seizure, pre-existing hypertension, ischemic vascular diseases, with known porphyria, in patients with myeloid malignant tumor, with chronic liver failure and in patients with increased baseline hemoglobin level (greater than 130g/L). In addition, the level of iron and vitamin B12 level should be evaluated. In case of iron and vitamin shortage, supplements should be administered prior to erythropoietin therapy.

Side effects

The most common side effects of erythropoietin are severe cutaneous adverse reactions (SCAR) and Stevens Johnsons Syndrome. Other side effects includes in patients with CKD are hypertension, arthralgia, muscle spasm, pyrexia, dizziness, medical device malfunction, vascular occlusion, and upper respiratory tract infection. The side effects included in patients with cancer chemotherapy are nausea, vomiting, myalgia, arthralgia, stomatitis, cough, weight decrease, leukopenia, bone pain, rash, hyperglycemia, insomnia, headache, depression, dysphagia and hypokalemia. These side effects included in case of ziduvudine treated HIV infected patients are pyrexia, cough, rash, and injection site irritation. The side effects included in surgery patients are nausea, vomiting, pruritus, headache, injection site pain, chills, deep vein thrombosis, cough and hypertension.

Use in pregnancy and lactation

Pregnancy: Erythropoietin alfa is pregnancy category C drug. There are no adequate and well controlled studies of erythropoietin alfa in pregnant woman. Consequently in pregnant patients with chronic renal failure, erythropoietin should only be used if the potential benefit outweighs the potential risk to the fetus. In pregnancy surgical patients participating in an autologous blood predonation program, use of erythropoietin alfa is not recommended

Lactation: It is not known whether exogenous erythropoietin alfa is excreted in human milk. Thus erythropoietin alfa should be used with caution in nursing mother. In lactating surgical patients participating in an autologous blood predonation program, use of erythropoietin alfa is not recommended.

Use in children and adolescents

Erythropoietin alfa is indicated in pediatric patients of 1 month to 16 years of age for treatment of anemia associated with CKD requiring dialysis.

Drug interaction

Drug interaction with medication: There is no evidence that treatment with erythropoietin alfa alters the metabolism of other medicinal products. However, there is a potential chance for interaction with cyclosporine. In addition, using lenalidomide, thalidomide or pomalidomide together with erythropoietin alfa may increase the risk of dangerous blood clots. The risk is higher in case of using lenalidomide with dexamethasone for the treatment of multiple myeloma than using lenalidomide alone for some other condition.

Drug interaction with foods: Not applicable

Drug interaction with others: Not applicable

Overdose

Erythropoietin has a very wide safety margin. Overdose symptoms are associated with rapid increase of hemoglobins. Patients with overdose should be closely monitored for cardiovascular and hematologic abnormalities. When the hemoglobin level is extremely high, phlebotomy may provide the solution. Cases of severe hypertension have been observed following overdose with erythropoietin.

Storage

Store in a 2°C to 8°C (in a refrigerator), protected from light. Keep away from the reach of children. Do not shake and do not keep in deep fridge

Packing

Recogen® 2000 IU: Each box contains 1 prefilled syringe with a needle, needle cap and a needle safety guard attached to the syringe containing 0.5 ml sterile solution of 2000 IU of recombinant human Erythropoietin alfa BP, a pair of hand gloves, a first aid bandage and an alcohol pad

Recogen® 3000 IU: Each box contains 1 prefilled syringe with a needle, needle cap and a needle safety guard attached to the syringe containing 0.75 ml sterile solution of 3000 IU of recombinant human Erythropoietin alfa BP, a pair of hand gloves, a first aid bandage and an alcohol pad.

Recogen® 5000 IU: Each box contains 1 prefilled syringe with a needle, needle cap and a needle safety guard attached to the syringe containing 0.5 ml sterile solution of 5000 IU of recombinant human Erythropoietin alfa BP, a pair of hand gloves, a first aid bandage and an alcohol pad.

Recogen® 10000 IU: Each box contains 1 prefilled syringe with a needle, needle cap and a needle safety guard attached to the syringe containing 1 ml sterile solution of 10000 IU of recombinant human Erythropoietin alfa BP, a pair of hand gloves, a first aid bandage and an alcohol pad.



ACI Limited

Godnyl, Narayanganj, Bangladesh