Eporise

Erythropoietin

COMPOSITION:

Eporise 2000 IU Injection: Each pre-filled syringe contains 0.5 ml sterile solution of Erythropoietin Concentrated Solution BP equivalent to Erythropoietin 2000 IU.

Eporise 3000 IU Injection: Each pre-filled syringe contains 0.75 ml sterile solution of Erythropoietin Concentrated Solution BP equivalent to Erythropoietin 3000 IU.

Eporise 5000 IU Injection: Each pre-filled syringe contains 0.5 ml sterile solution of Erythropoietin Concentrated Solution BP equivalent to Erythropoietin 5000 IU.

PHARMACOLOGY:

Erythropoietin alfa is recombinant human erythropoietin (EPO). It is expressed in Chinese hamster ovary cells and has a 165 amino acid sequence identical to that of human urinary EPO; the two are indistinguishable on the basis of functional assays. The apparent molecular weight of erythropoietin is about 30,400 daltons. Erythropoietin stimulates erythropoiesis by the same mechanism as endogenous erythropoietin. Erythropoietin increases the reticulocyte count, followed by increases in the RBC count, hemoglobin, and hematocrit.

INDICATIONS:

Erythropoietin alfa is an erythropoiesis-stimulating agent (ESA) indicated for:

Treatment of anemia due to:

- Chronic Kidney Disease (CKD) in patients on dialysis and not on dialysis.
- Zidovudine in HIV-infected patients.
- The effects of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.
- Reduction of allogeneic RBC transfusions in patients undergoing elective, noncardiac, nonvascular surgery.

DOSAGE AND ADMINISTRATION:

Evaluation of Iron Stores and Nutritional Factors:

Evaluate the iron status in all patients before and during treatment and maintain iron repletion. Correct or exclude other causes of anemia (e.g., vitamin deficiency, metabolic or chronic inflammatory conditions, bleeding, etc.) before initiating Erythropoietin alfa.

Patients with Chronic Kidney Disease

For all patients with CKD:

When initiating or adjusting therapy, monitor hemoglobin levels at least weekly until stable, then monitor at least monthly. When adjusting therapy consider hemoglobin rate of rise, rate of decline, ESA responsiveness and hemoglobin variability. A single hemoglobin excursion may not require a dosing change.

- Do not increase the dose more frequently than once every 4 weeks. Decreases in dose can occur more frequently. Avoid frequent dose adjustments.
- If the hemoglobin rises rapidly (e.g., more than 1 g/dL in any 2-week period), reduce the dose of Erythropoietin alfa by 25% or more as needed to reduce rapid responses.
- For patients who do not respond adequately, if the hemoglobin has not increased by more than 1 g/dL after 4 weeks of therapy, increase the dose by 25%.
- For patients who do not respond adequately over a 12-week escalation period, increasing the Erythropoietin alfa dose further is unlikely to improve response and may increase risks. Use the lowest dose that will maintain a hemoglobin level sufficient to reduce the need for RBC transfusions. Evaluate other causes of anemia. Discontinue Erythropoietin alfa if responsiveness does not improve.

For patients with CKD on dialysis:

- Initiate Erythropoietin alfa treatment when the hemoglobin level is less than 10 g/dL.
- If the hemoglobin level approaches or exceeds 11 g/dL, reduce or interrupt the dose of Erythropoietin alfa.
- The recommended starting dose for adult patients is 50 to 100 units/kg 3 times weekly intravenously or subcutaneously. For pediatric patients, a starting dose of 50 units/kg 3 times weekly intravenously or subcutaneously is recommended. The intravenous route is recommended for patients on hemodialysis.

For patients with CKD not on dialysis:

- Consider initiating Erythropoietin alfa treatment only when the hemoglobin level is less than 10 g/dL and the following considerations apply:
- The rate of hemoglobin decline indicates the likelihood of requiring a RBC transfusion and,
- Reducing the risk of alloimmunization and/or other RBC transfusion-related risks is a goal.
- If the hemoglobin level exceeds 10 g/dL, reduce or interrupt the dose of Erythropoietin alfa, and use the lowest dose of Erythropoietin alfa sufficient to reduce the need for RBC transfusions.
- The recommended starting dose for adult patients is 50 to 100 units/kg 3 times weekly intravenously or subcutaneously.

Zidovudine-treated HIV-infected Patients

Starting Dose

The recommended starting dose in adults is 100 units/kg as an intravenous or subcutaneous injection 3 times per week.

Dose Modification

- If hemoglobin does not increase after 8 weeks of therapy, increase Erythropoietin alfa dose by approximately 50 to 100 units/kg at 4-to 8-week intervals until hemoglobin reaches a level needed to avoid RBC transfusions or 300 units/kg.
- Withhold Erythropoietin alfa if hemoglobin exceeds 12 g/dL. Resume therapy at a dose 25% below the previous dose when hemoglobin declines to less than 11 g/dL.

Discontinue Erythropoietin alfa if an increase in hemoglobin is not achieved at a dose of 300 units/kg for 8 weeks.

Patients on Cancer Chemotherapy

Initiate Erythropoietin alfa in patients on cancer chemotherapy only if the hemoglobin is less than 10 g/dL, and if there is a minimum of two additional months of planned chemotherapy. Use the lowest dose of Erythropoietin alfa necessary to avoid RBC transfusions.

Recommended Starting Dose

Adults:

- 150 units/kg subcutaneously 3 times per week until completion of a chemotherapy course or
- 40,000 units subcutaneously weekly until completion of a chemotherapy course.

Pediatric Patients (5 to 18 years):

- 600 units/kg intravenously weekly until completion of a chemotherapy course.

Surgery Patients

The recommended Erythropoietin alfa regimens are:

- 300 units/kg per day subcutaneously for 15 days total: administered daily for 10 days before surgery, on the day of surgery, and for 4 days after surgery.
- 600 units/kg subcutaneously in 4 doses administered 21, 14, and 7 days before surgery and on the day of surgery. Deep venous thrombosis prophylaxis is recommended during Erythropoietin alfa therapy.

CONTRAINDICATIONS:

- Uncontrolled hypertension.
- Serious allergic reactions to Erythropoietin alfa.
- Patients who develop Pure Red Cell Aplasia (PRCA) following treatment with any erythropoietin should not receive eporise or any other erythropoietin.

WARNINGS AND PRECAUTIONS:

- Increased Mortality, Myocardial Infarction, Stroke, and Thromboembolism
- Increased Mortality and/or Increased Risk of Tumor Progression or Recurrence in Patients With Cancer
- Hypertension
- Seizures
- Lack or Loss of Hemoglobin Response to Erythropoietin alfa
- Pure Red Cell Aplasia
- Serious Allergic Reactions
- Severe Cutaneous Reactions

ADVERSE REACTIONS:

Adverse reactions in 5% of Erythropoietin alfa treated patients in clinical studies were:

- Patients with CKD: Hypertension, arthralgia, muscle spasm, pyrexia, dizziness, medical device malfunction, vascular occlusion, and upper respiratory tract infection.
- Zidovudine-treated HIV-infected Patients: Pyrexia, cough, rash, and injection site irritation.
- Cancer Patients on Chemotherapy: Nausea, vomiting, myalgia, arthralgia, stomatitis, cough, weight decrease, leukopenia, bone pain, rash, hyperglycemia, headache, depression, dysphagia, hypokalemia, and thrombosis.
- Surgery Patients: Nausea, vomiting, pruritus, headache, injection site pain, chills, deep vein thrombosis, cough, and hypertension.
- Premature infants: A fall in serum ferritin values is very common (>10%)

USE IN SPECIAL POPULATION:

Pregnancy

Erythropoietin alfa from multiple-dose vials contains benzyl alcohol and is contraindicated in pregnant women. When therapy with Erythropoietin alfa is needed during pregnancy, use a benzyl alcohol-free formulation

Lactation

Erythropoietin alfa from multiple-dose vials contains benzyl alcohol and is contraindicated in lactating women. Advise a lactating woman not to breastfeed for at least 2 weeks after the last dose.

Pediatric Use

When therapy with Erythropoietin alfa is needed in neonates and infants, use the single-dose vial, which is a benzyl alcohol-free formulation.

Geriatric Use

No overall differences in safety or effectiveness were observed between geriatric and younger patients.

DRUG INTERACTION:

There are no known clinically significant drug interactions of Erythropoietin alfa.

OVERDOSE:

The therapeutic margin of Erythropoietin alfa is very wide. Erythropoietin alfa overdosage can cause hemoglobin levels above the desired level, which should be managed with discontinuation or reduction of Erythropoietin alfa dosage and/or with phlebotomy, as clinically indicated. Cases of severe hypertension have been observed following overdose with ESAs.

STORAGE:

Store at 2°C to 8°C. Do not freeze or shake. This temperature range should be closely maintained until administration to the patient. Store in original package in order to protect from light.

COMMERCIAL PACKAGING:

Eporise 2000 IU injection: Each box contains 1 pre-filled syringe of 0.5 ml sterile solution of Erythropoietin 2000 IU injection and an alcohol pad.

Eporise 3000 IU injection: Each box contains 1 pre-filled syringe of 0.75 ml sterile solution of Erythropoietin 3000 IU injection and an alcohol pad.

Eporise 5000 IU injection: Each box contains 1 pre-filled syringe of 0.5 ml sterile solution of Erythropoietin 5000 IU injection and an alcohol pad.

Manufactured by:

ZISKA PHARMA

Ziska Pharmaceuticals Ltd.

Kaliakoir, Gazipur, Bangladesh

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