

Erythropoietin (Epoetin Beta) instructions

translated from original Russian instructions by Extrapharmacy Online Store

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Name in Cyrillic : Эритропое́тин

1 ml of the solution contains:

Active substance: Recombinant human erythropoietin 2000 IU

Excipients: Albumin solution 10% - 2.5 mg,

Isotonic citrate buffer: sodium citrate -5.8 mg, sodium chloride-5.84 mg, citric acid-0.057 mg, water for injection-up to 1 ml.

Pharmacologic action

The administration of epoetin beta leads to an increase in hemoglobin and hematocrit, an improvement in the blood supply of tissues and the work of the heart. The most pronounced effect of epoetin beta is observed in anemia caused by chronic renal insufficiency. In very rare cases, with the long-term use of erythropoietin for the therapy of anemic conditions, the formation of neutralizing antibodies to epoetin beta can be observed with the development of partial red cell aplasia or without it.

When using Erythropoietin in women of reproductive age it is possible to resume menstruation. The patient should be warned about the possibility of pregnancy and the need for reliable methods of contraception before the start of therapy.

Considering the possible more pronounced effect of Erythropoietin, its dose should not exceed the dose of epoetin beta used in the previous course of treatment. During the first two weeks, the dose is not changed, the dose / response ratio is evaluated. After that the dose can be reduced or increased.

During the treatment period, before the optimal maintenance dose is established, patients with uremia should avoid practicing potentially dangerous activities that require an increased concentration of attention and speed of psychomotor reactions, because of the increased risk of high blood pressure at the beginning of therapy.

Pharmacokinetics

With intravenous administration of erythropoietin in healthy individuals and patients with uremia, the half-life period is 5-6 hours. With subcutaneous administration of erythropoietin its concentration in the blood increases slowly and reaches a maximum in the period from 12 to 28 hours after administration, the half-life is 13-28 hours. At intravenous introduction the half-life period makes 4-12 hours. Bioavailability of Erythropoietin at subcutaneous administration is 25-40%.

Indications

- Treatment of anemia of renal genesis in patients with chronic renal failure, incl. who are on dialysis.
- Prevention and treatment of anemia in adult patients with solid tumors receiving chemotherapy with platinum preparations that can cause anemia (carboplatin 75 mg / m² per cycle, carboplatin 350 mg / m² per cycle).
- Treatment of anemia in adults with myeloma, low-grade non-Hodgkin's lymphomas and chronic lymphocytic leukemia, receiving antitumor therapy with relative deficiency of endogenous erythropoietin (defined as serum erythropoietin concentration, disproportionately low relative to the degree of anemia).
- An increase in the volume of donor blood intended for subsequent autotransfusion. However the benefits of epoetin beta should be correlated with an increased risk of thromboembolism when it is used. Patients with moderate anemia (hemoglobin level 100-130 g / l or hematocrit 30-39%, without iron deficiency) the drug is prescribed only if it is not possible to get sufficient amount of preserved blood, and planned large surgical intervention may require a large volume blood (> 4 units for women or > 5 units for men).
- Prevention of anemia in premature newborns born with a body weight of 750-1500 g, up to 34 weeks of gestation.

Contraindications

Hypersensitivity to the drug or its components, partial red cell aplasia after previous therapy with any epoetin beta, uncontrolled hypertension, inability to conduct adequate anticoagulant therapy, myocardial infarction within a month after the event, unstable angina or an increased risk of deep vein thrombosis and thromboembolism in the pre-release blood collection program before surgical operations, porphyria.

With caution

In patients with thrombosis (in the anamnesis), with malignant neoplasms, with sickle-cell anemia, with moderate anemia without iron deficiency, with thrombocytosis, with refractory anemia, epilepsy, chronic liver failure, nephrosclerosis, in patients with a body weight of less than 50 kg to increase volume donor blood for subsequent autotransfusion.

Pregnancy and breast-feeding

Since there is no sufficient experience with the use of erythropoietin during pregnancy and during breast-feeding in humans, Erythropoietin should be prescribed only if the expected benefits from its use exceed the possible risk to the fetus and the mother.

Side effects

Cardiovascular system: in patients with anemia with chronic renal insufficiency, the most frequent is an increase in arterial pressure or an increase in the existing arterial hypertension, especially in the case of a rapid increase in hematocrit. In this case it is recommended to prescribe medicinal antihypertensive therapy, in the absence of effect it is recommended to temporarily interrupt epoetin beta therapy. Some patients (including those with normal or low blood pressure earlier) have a hypertensive crisis with encephalopathy (headaches, confusion, sensory and motor disorders - speech disorders, gait, up to tonic-clonic seizures) requiring urgent medical attention care and intensive care. Particular attention should be paid to sudden migraine-like pain.

In patients with solid tumors, myeloma, non-Hodgkin's lymphomas or chronic lymphocytic leukemia headaches may rarely be noted, an increase in blood pressure that can be stopped by the appointment of a drug.

Hemopoiesis: in patients with renal insufficiency and anemia, a dose-dependent increase in the number of platelets (not exceeding the norm and disappearing with the continuation of therapy), especially after IV introduction, may occur. Very rarely thrombocytosis develops. Because of the increase in hematocrit, it is often necessary to increase the dose of heparin during hemodialysis. With inadequate heparinization a blockage of the dialysis system is possible. Shunt thrombosis may develop, especially in patients with a tendency to hypotension or with complications of arteriovenous fistula (eg stenosis, aneurysm, etc.). In such situations an early revision of the shunt and the timely prevention of thrombosis (acetylsalicylic acid) are recommended.

In most cases simultaneously with an increase in hematocrit serum ferritin levels decrease. In some cases, patients with uremia - increased levels of potassium and phosphate in the serum.

Interaction

With the simultaneous use of Erythropoietin and Cyclosporine, it may be necessary to correct the dose of Cyclosporine due to an increase in its binding by red blood cells. The experience of the clinical use of Erythropoietin has so far not revealed the facts of its pharmacological incompatibility with other medications. However in order to avoid possible incompatibility or decrease in activity Erythropoietin should not be mixed with solutions of other medications.

Dosing and Administration

Treatment of anemia in patients with chronic renal failure.

Subcutaneously or intravenously.

With intravenous administration the solution should be administered within 2 minutes, for patients on hemodialysis - through the arteriovenous shunt at the end of the dialysis session. Patients who are not on hemodialysis – subcutaneous administration is preferable to avoid puncture of peripheral veins.

The goal of the treatment is to achieve a level of hematocrit equal to 30-35%, or elimination of the need for blood transfusion. The weekly increase in hematocrit should not exceed 0.5%. Do not exceed his level of 35%. In patients with hypertension, cardiovascular and cerebrovascular diseases - the weekly increase in hematocrit and its targets should be determined individually, depending on the clinical picture. For some patients, the optimal hematocrit value is below 30%.

Treatment with Erythropoietin is carried out in 2 stages:

Initial therapy (correction stage)

With subcutaneous administration the initial dose is 20 IU / kg body weight 3 times a week. If there is insufficient increase in hematocrit (less than 0.5% per week) - the dose can be increased monthly by 20 IU / kg of body weight 3 times a week. The total weekly dose can also be divided into daily injections in smaller doses or administered at one time.

When intravenously administered, the initial dose is 40 IU / kg body weight 3 times a week. If the hematocrit is not increased enough, the dose can be increased to 80 IU / kg 3 times a week in a month. If there is a need to further increase the dose, it should be increased by 20 IU / kg 3 times a week at a monthly interval. Regardless of the method of administration, the highest dose is not more than 720 IU / kg body weight per week.

Supportive therapy

To maintain hematocrit at 30-35%, first dose should be reduced by half from the dose in the previous injection. Subsequently, the maintenance dose is selected individually, with an interval of 1-2 weeks. With subcutaneous administration, a weekly dose can be administered once or for 3-7 administrations per week.

In children, the dose depends on age (usually the smaller the age of the child, the higher the dose of epoetin beta is required). However, since it is not possible to predict an individual response, it is advisable to begin with the recommended regimen.

Prevent anemia in premature newborns

Subcutaneously in a dose of 250 IU / kg body weight 3 times a week. Treatment with epoetin beta should begin as soon as possible, preferably from 3 days of life and last for 6 weeks.

Prevention and treatment of anemia in patients with solid tumors

Subcutaneously, dividing the weekly dose into 3-7 injections.

Patients with solid tumors receiving chemotherapy with platinum drugs, treatment with erythropoietin is indicated at a hemoglobin level before chemotherapy is not higher than 130 g / l. The initial dose is 450 IU / kg of body weight per week. If after 4 weeks the hemoglobin level does not increase enough - the dose should be doubled. Duration of treatment - no more than 3 weeks after the end of chemotherapy. If during the first cycle of chemotherapy the hemoglobin level, despite epoetin beta treatment, decreases by more than 10 g / l, further use of the drug may not be effective.

It should avoid increasing hemoglobin by more than 20 g / l per month or up to a level above 140 g / l.

When the hemoglobin increases by more than 20 g / L per month, the dose of epoetin beta should be reduced by 50%. If the hemoglobin level exceeds 140 g / l, the drug is canceled until it falls to <120 g / l, and then resumes therapy at a dose that is half the previous week.

Treatment of anemia in patients with myeloma, low-grade non-Hodgkin's lymphoma or chronic lymphocytic leukemia

In patients with myeloma, low-grade non-Hodgkin's lymphoma or chronic lymphocytic leukemia inadequacy of endogenous erythropoietin is usually noted. It is diagnosed by the ratio between the degree of anemia

and the inadequate concentration of erythropoietin in the serum.

At a level of hemoglobin (g / l)	Concentration of erythropoietin in serum (IU / ml)
> 90 <100	≤ 100
> 80 ≤ 90	≤ 180
≤ 80	≤ 300

The above parameters should be determined not earlier than 7 days after the last blood transfusion and the last cycle of cytotoxic chemotherapy.

The drug is administered subcutaneously; a weekly dose can be divided into 3 or 7 injections. The recommended initial dose is 450 IU / kg body weight per week. If after 4 weeks the hemoglobin level rises by at least 10 g / l - the treatment is continued at the same dose. If after 4 weeks the hemoglobin rises by less than 10 g / l - you can increase the dose to 900 IU / kg body weight per week. If after 8 weeks of treatment the hemoglobin level did not increase by at least 10 g / l - a positive effect is unlikely and the drug should be discontinued.

Clinical studies have shown that with chronic lymphocytic leukemia the response to epoetin beta therapy occurs two weeks later than in patients with myeloma, non-Hodgkin's lymphoma and solid tumors. Treatment should continue until 4 weeks after the end of chemotherapy.

The highest dose should not exceed 900 IU / kg of body weight per week. If for 4 weeks of treatment the hemoglobin level increases by more than 20 g / l - the dose of Erythropoietin should be reduced by half. If the hemoglobin level exceeds 140 g / l - treatment with the drug should be interrupted until it drops to <130 g / l, after which the therapy is resumed at a dose that is half the previous week. Treatment should be resumed only if the most likely cause of anemia is the failure of Erythropoietin.

Preparation of patients for the collection of donor blood for subsequent autohemotransfusion

Intravenously or subcutaneously twice a week for 4 weeks. In those cases when the hematocrit value of the patient (> 33%) allows blood sampling, epoetin beta is administered at the end of the procedure. Throughout the course of treatment, the hematocrit should not exceed 48%.

The dose of the drug is determined by the transfusiologist and the surgeon individually, depending on how much blood is taken from the patient and from his erythrocyte reserve.

The possibility of donation depends mainly on the volume of blood in this patient and the initial hematocrit. Both indices determine the endogenous red blood cell reserve, which can be calculated using the following formula:

endogenous erythrocyte reserve = volume of blood (ml) x (hematocrit - 33): 100

women: blood volume (ml) = 41 (ml / kg) x body weight (kg) + 1200 (ml)

men: blood volume (ml) = 44 (ml / kg) x body weight (kg) + 1600 (ml) (with body weight > 45 kg).

Indications for use Erythropoietin and its single dose are determined from nomograms, based on the required volume of donor blood and endogenous red blood cell.

The highest dose - with intravenous administration no more than 1600 IU / kg body weight per week; when administered subcutaneously, 1200 IU / kg body weight per week.

Special instructions

Since in some cases anaphylactoid reactions have been observed, the first dose of the drug should be administered under the supervision of a physician.

Inadequate use of the drug by healthy people (for example as a dope) can cause a sharp increase in the hematocrit, accompanied by life-threatening complications from the cardiovascular system.

During treatment, it is necessary to monitor blood pressure weekly and conduct a general blood test, including determination of hematocrit, platelets and ferritin. In the first 8 weeks of therapy, a weekly count of the elements and especially the platelets is needed. With an increase in the number of platelets above the norm or more than $150 - 109 / L$ from the initial value, treatment with erythropoietin should be discontinued.

In patients with uremia who are on hemodialysis, it is recommended to monitor blood pressure, incl. between dialysis sessions. Because of the increase in hematocrit it is often necessary to increase the dose of heparin, in addition timely prevention of thrombosis and early revision of the shunt is necessary. In the pre- and postoperative period, hemoglobin should be monitored more often if its baseline level is less than 140 g / l . During treatment with Erythropoietin it is necessary to periodically monitor the level of potassium and phosphate in the blood serum. When hyperkalemia occurs it is necessary to temporarily cancel Erythropoietin before the normalization of the potassium concentration.

In most cases simultaneously with an increase in hematocrit serum ferritin levels decrease. Therefore all patients with anemia of renal genesis and with a serum ferritin level of less than $100 \mu\text{g / l}$ or transferrin saturation of less than 20% are recommended to receive oral iron at a dose of $200-300 \text{ mg / day}$. Patients with oncological and hematological diseases receive iron therapy according to the same principles and patients with myeloma, non-Hodgkin's low-grade lymphoma or chronic lymphocytic leukemia with transferrin saturation less than 25% can be administered 100 mg of iron per week intravenously.

For preterm infants oral iron therapy at a dose of 2 mg per day should be given as early as possible (no later than 14 days of life). The dose of iron is corrected depending on the level of serum ferritin. If it persistently remains below 100 mcg / ml or there are other signs of iron deficiency the dose of iron preparations should be increased to $5-10 \text{ mg / day}$ and therapy should be performed until the symptoms of iron deficiency are relieved.

Overdose

Symptoms: hypertension, erythrocytosis, hyperhemoglobinemia, a sharp increase in hematocrit.

Treatment: symptomatic. In the case of hypertension, excessive hydration should be avoided. In the presence of erythrocytosis and hyperhydration, measures are needed to remove excess fluid.

With a high level of hemoglobin and hematocrit phlebotomy is indicated.

Manufacturer : BinnoPharm (Russia)

Reliable supplier with fast Worldwide shipping

Extrapharmacy Online Store

<http://extrapharmacy.ru>

Storage

$+2 \dots +8 \text{ } ^\circ \text{C}$.

Keep out of the reach of children.

Shelf-life of the drug is 2 years.