CLINICAL UPDATE

Brand Name	Retacrit™
Generic Name	epoetin alfa-epbx
Drug Manufacturer	Hospira, Inc

Clinical Update

TYPE OF CLINICAL UPDATE

New Formulation and Strength

FDA APPROVAL DATE

June 30, 2020

LAUNCH DATE

November 23, 2020

REVIEW DESIGNATION

N/A

TYPE OF REVIEW

Biologic License Application (BLA): 125545

DISPENSING RESTRICTIONS

Speciality Pharmacy

Overview

INDICATION(S) FOR USE

Retacrit™ 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 patients with HIV-infection.
  - 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.

MECHANISMS OF ACTION

Epoetin alfa induces erythropoiesis by stimulating the division and differentiation of committed erythroid progenitor cells and induces the release of reticulocytes from the bone marrow into the bloodstream, where they mature to erythrocytes. There is a dose response relationship with this effect. This results in an increase in reticulocyte counts followed by a rise in hematocrit and hemoglobin levels.

DOSAGE FORM(S) AND STRENGTH(S)

Injection

- Single-dose vials: 2,000 Units/mL, 3,000 Units/mL, 4,000 Units/mL, and 10,000 Units/mL

- Multiple-dose vials: 20,000 Units/2 mL (10,000 Units/mL) and 20,000 Units/mL containing benzyl alcohol

DOSE & ADMINISTRATION

- Evaluate iron status before and during treatment and maintain iron repletion. Correct or exclude other causes of anemia before initiating treatment.
- In pregnant women, lactating women, neonates, infants: Use only single-dose vials.
- Patients with CKD: Initial dose: 50 to 100 Units/kg 3 times weekly (adults) and 50 Units/kg 3 times weekly (pediatric patients). Individualize maintenance dose. Intravenous route recommended for patients on hemodialysis.
- Patients on Zidovudine due to HIV-infection: 100 Units/kg 3 times weekly.
- Patients with Cancer on Chemotherapy: 40,000 Units weekly or 150 Units/kg 3 times weekly (adults); 600 Units/kg intravenously weekly (pediatric patients ≥ 5 years).
- Surgery Patients: 300 Units/kg per day daily for 15 days or 600 Units/kg weekly.

EFFICACY

Adult Patients on Dialysis

Patients with chronic kidney disease on dialysis: ESA effects on rates of transfusion

In clinical studies of patients with CKD on dialysis, epoetin alfa increased hemoglobin levels and decreased the need for RBC transfusion. Overall, more than 95% of patients were RBC transfusion independent after receiving epoetin alfa for 3 months. In clinical studies at starting doses of 50 to 150 Units/kg 3 times weekly, adult patients responded with an average rate of hemoglobin rise as presented in Table.

Starting Dose (3 Times Weekly Intravenously)	Hemoglobin Increase in 2 Weeks
50 Units/kg	0.5 g/dL
100 Units/kg	0.8 g/dL
150 Units/kg	1.2 g/dL

The safety and efficacy of epoetin alfa were evaluated in 13 clinical studies involving intravenous administration to a total of 1010 patients on dialysis with anemia. Overall, more than 90% of the patients treated with epoetin alfa experienced improvement in hemoglobin concentrations. In the 3 largest of these clinical studies, the median maintenance dose necessary to maintain the hemoglobin between 10 to 12 g/dL was approximately 75 Units/kg 3 times weekly. More than 95% of patients were able to avoid RBC transfusions. In the largest US multicenter study, approximately 65% of the patients received doses of 100 Units/kg 3 times weekly or less to maintain their hemoglobin at approximately 11.7 g/dL. Almost 10% of patients received a dose of 25 Units/kg or less, and approximately 10% received a dose of more than 200 Units/kg 3 times weekly to maintain their hemoglobin at this level.

In the Normal Hematocrit Study, the yearly transfusion rate was 51.5% in the lower hemoglobin group (10 g/dL) and 32.4% in the higher hemoglobin group (14 g/dL).

Pediatric Patients with CKD on Dialysis

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The safety and efficacy of epoetin alfa were studied in a placebo-controlled, randomized study of 113 pediatric patients with anemia (hemoglobin ≤ 9 g/dL) undergoing peritoneal dialysis or hemodialysis. The initial dose of epoetin alfa was 50 Units/kg intravenously or subcutaneously 3 times weekly. The dose of study drug was titrated to achieve either a hemoglobin of 10 to 12 g/dL or an absolute increase in hemoglobin of 2 g/dL over baseline. At the end of the initial 12 weeks, a statistically significant rise in mean hemoglobin (3.1 g/dL vs. 0.3 g/dL) was observed only in the epoetin alfa arm. The proportion of pediatric patients achieving a hemoglobin of 10 g/dL, or an increase in hemoglobin of 2 g/dL over baseline, at any time during the first 12 weeks was higher in the epoetin alfa arm (96% vs. 58%). Within 12 weeks of initiating epoetin alfa therapy, 92.3% of the pediatric patients were RBC transfusion independent as compared to 65.4% who received placebo. Among patients who received 36 weeks of epoetin alfa, hemodialysis patients received a higher median maintenance dose [167 Units/kg/week (n = 28) vs. 76 Units/kg/week (n = 36)] and took longer to achieve a hemoglobin of 10 to 12 g/dL (median time to response 69 days vs. 32 days) than patients undergoing peritoneal dialysis.