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DTC ➔ ERYTHROPOIETIN (*PROCRIT*; *EPOGEN*) REVISITED

Use of epoetin alfa (*Procrit* – Ortho Biotech; *Epogen* – Amgen), a recombinant human erythropoietin (Medical Letter 1989; 31:85), is being promoted directly to consumers in vague advertisements that promise renewed energy and improved work capacity. Epoetin is approved by the FDA for treatment of anemia due to chronic renal failure, cancer chemotherapy or HIV treatment, and before elective non-cardiac surgery. It is also used illicitly by competitive athletes to increase their endurance.

INDICATIONS – Renal Failure – Erythropoietin use in patients with renal failure decreases cardiovascular morbidity and mortality and improves quality of life (D Tsakiris, *Nephron* 2000; 85 suppl 1:2). Guidelines for the management of anemia associated with chronic renal failure recommend maintaining the hematocrit in the range of 33% to 36% (National Kidney Foundation—Dialysis Outcomes Quality Initiative, *Am J Kidney Dis* 2001; 37 suppl 1:S182). Hematocrits lower than 30% to 33% and higher than 40% have been associated with decreased survival (RN Foley et al, *Am J Kidney Dis* 1996; 28:53; A Besarab et al, *N Engl J Med* 1998; 339:584).

Cancer – Epoetin treatment of anemic patients undergoing chemotherapy for nonmyeloid malignancies has increased hemoglobin by about 2 g/dL and decreased the need for transfusions. Patients' energy, activity level and quality of life improved as hemoglobin rose; the greatest improvement in quality of life occurred when hemoglobin increased from 11 to 12 g/dL (J Glaspy et al, *J Clin Oncol* 1997; 15:1218; GD Demetri et al, *J Clin Oncol* 1998; 16:3412; CS Cleeland et al, *Proc Am Soc Clin Oncol* 1999; 18:574a abstract 2215).

HIV Infection – HIV disease and its treatment, particularly with zidovudine, can cause anemia. Epoetin use increases hematocrit, decreases transfusion requirements and increases energy in these patients (DH Henry et al, *Ann Intern Med* 1992; 117:739; DA Revicki et al, *J Acquir Immune Defic Syndr* 1993; 7:474), and has prolonged survival in AIDS patients with anemia (RD Moore, *Clin Infect Dis* 1999; 29:44). In one study of AIDS patients with anemia, epoetin was as effective in patients who were not taking zidovudine as it was in those who were taking the drug (HH Balfour et al, *Int J Antimicrob Agents* 1997; 8:189). Epoetin generally has not raised hemoglobin concentrations or decreased transfusion requirements in patients with erythropoietin concentrations higher than 500 mU/mL.

Surgery and Autologous Blood Donations – A randomized trial in patients with baseline hematocrit \leq 39% found that epoetin use before surgery increased the number of units of

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blood patients were able to predeposit and decreased the need for transfusions after surgery (TH Price et al, *Transfusion* 1996; 36:29). A placebo-controlled trial before major orthopedic surgery found that patients with a baseline hemoglobin of 10 to 13 g/dL who were treated with epoetin required fewer transfusions (JR de Andrade et al, *Am J Orthop* 1996; 25:533).

ADVERSE EFFECTS — Hypertension occurs in about 25% of patients with renal disease who are treated with the drug. Hypertensive encephalopathy and seizures occur rarely. Thrombotic events including myocardial infarction and clotting of arteriovenous fistulas and shunts have also occurred. In patients with cancer or HIV infection, the drug has generally been well tolerated.

DOSAGE — Epoetin is available in single-dose vials of 2000, 3000, 4000, 10,000, 20,000 or 40,000 units or in multi-dose vials. In most clinical trials, the drug was injected three times a week. Once-weekly use, which is a recommended alternative before surgery, is common in other patients as well, but almost no published data are available (FDC Reports 2001; 63[5]:20; JL Gabrilove et al, *Proc Am Soc Clin Oncol* 1999; 18:574A, abstract 2216).

For patients with **chronic renal failure**, the manufacturer recommends a starting dose of 50 to 100 U/kg three times a week (TIW) either intravenously or subcutaneously. The dosage may be increased if the hematocrit does not rise by 5 to 6 points after eight weeks of treatment. To minimize the risk of hypertension, the dose should be decreased or stopped when the hematocrit approaches 36% or increases by more than 4 points in a two-week period. Epoetin is not recommended for **cancer patients** receiving chemotherapy unless the baseline serum erythropoietin level is less than 200 mU/mL; the recommended starting dose is 150 U/kg TIW subcutaneously. For **HIV patients** taking zidovudine, treatment with epoetin 100 U/kg TIW intravenously or subcutaneously is recommended when the serum erythropoietin level is less than 500 mU/mL. If the response is not satisfactory after eight weeks of treatment, the dose can be increased in 50 to 100 U/kg increments for both cancer and HIV patients to a total of 300 U/kg.

COST — The cost for a 10,000 U vial of *Epogen* is \$124.68 and for a 40,000 U vial of *Procrit* is \$516.18, according to AWP listings in *Drug Topics Red Book Update*, May 2001. Eight weeks' treatment of a 70-kg cancer patient with the starting dose of 150 U/kg TIW (three 10,000-unit vials) would cost about \$3000 for the drug alone.

CONCLUSION — Within limits narrower than direct-to-consumer (DTC) advertisements would suggest, injection of epoetin alfa appears to be worthwhile for treating anemia due to renal failure, HIV infection or cancer chemotherapy.

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