Cyanocobalamin is quantitatively and rapidly absorbed from intramuscular and subcutaneous sites of injection; the plasma level of the compound reaches its peak within 1 hour after intramuscular injection. Absorbed vitamin B12 is transported via specific B12 binding proteins, transcobalamin I and II to the various tissues. The liver is the main organ for vitamin B12 storage. Within 48 hours after injection of 100 or 1000 mcg of vitamin B12, 50 to 98% of the injected dose may appear in the urine. The major portion is excreted within the first eight hours. Intravenous administration results in even more rapid excretion with little opportunity for liver storage. Gastrointestinal absorption of vitamin B12 depends on the presence of sufficient intrinsic factor and calcium ions. Intrinsic factor deficiency causes pernicious anemia, which may be associated with subacute combined degeneration of the spinal cord. Prompt parenteral administration of vitamin B12 prevents progression of neurologic damage. The average diet supplies about 5 to 15 mcg/day of vitamin B12 in a protein-bound form that is available for absorption after normal digestion. Vitamin B12 is not present in foods of plant origin, but is abundant in foods of animal origin. In people with normal absorption, deficiencies have been reported only in strict vegetarians who consume no products of animal origin (including no milk products or eggs). Vitamin B12 is bound to intrinsic factor during transit through the stomach; separation occurs in the terminal ileum in the presence of calcium, and vitamin B12 enters the mucosal cell for absorption. It is then transported by the transcobalamin binding proteins. A small amount (approximately 1% of the total amount ingested) is absorbed by simple diffusion, but this mechanism is inadequate only with very large doses. Oral absorption is considered too undependable to rely on in patients with pernicious anemia or other conditions resulting in malabsorption of vitamin B12. Cyanocobalamin is the most widely used form of vitamin B12, and has hematopoietic activity apparently identical to that of the antianemia factor in purified liver extract. Hydroxycobalamin is equally as effective as cyanocobalamin, and they share the cobalamin molecular structure.
Laboratory Tests: During the initial treatment of patients with pernicious anemia, serum potassium must be observed closely the first 48 hours and potassium replaced if necessary. Hematocrit, reticulocyte count, vitamin B₁₂, folate and iron levels should be obtained prior to treatment. Hematocrit and reticulocyte counts should be repeated daily from the fifth to seventh days of therapy and then frequently until the hematocrit is normal. If folate levels are low, folic acid should also be administered. If reticulocytes have not increased after treatment or if reticulocyte counts do not continue at least twice normal as long as the hematocrit is less than 35%, diagnosis or treatment should be reevaluated. Repeat determinations of iron and folic acid may reveal a complicating illness that might inhibit the response of the marrow.

Patients with pernicious anemia have about 3 times the incidence of carcinoma of the stomach as the general population, so appropriate tests for this condition should be carried out when indicated.

Drug/Laboratory Test Interactions: Persons taking most antibiotics, methotrexate and pyrimethamine invalidate folic acid and vitamin B₁₂ diagnostic blood assays. Colchicine para-aminosalicylic acid and heavy alcohol intake for longer than 2 weeks may produce malabsorption of vitamin B₁₂.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long term studies in animals to evaluate carcinogenic potential have not been done. There is no evidence from long-term use in patients with pernicious anemia that cyanocobalamin is carcinogenic. Pernicious anemia is associated with an increased incidence of carcinoma of the stomach, but this is believed to be related to the underlying pathology and not to treatment with cyanocobalamin.

Pregnancy: Teratogenic Effects. Pregnancy Category C: Adequate and well-controlled studies have not been done in pregnant women. However, vitamin B₁₂ is an essential vitamin and requirements are increased during pregnancy. Amounts of vitamin B₁₂ that are recommended by the Food and Nutrition Board, National Academy of Science-National Research Council for pregnant women (4 mcg daily) should be consumed during pregnancy.

Nursing Mothers: Vitamin B₁₂ is known to be excreted in human milk. Amounts of vitamin B₁₂ that are recommended by the Food and Nutrition Board, National Academy of Science-National Research Council for lactating women (4 mcg daily) should be consumed during lactation.

Pediatric Use: Intake in children should be in the amount (0.5 to 3 mcg daily) recommended by the Food and Nutrition Board, National Academy of Science-National Research Council.

ADVERSE REACTIONS:

Generalized: Anaphylactic shock and death have been reported with administration of parenteral vitamin B₁₂ (See WARNINGS).

Cardiovascular: Pulmonary edema and congestive heart failure early in treatment; peripheral vascular thrombosis.

Hematological: Polycythemia vera

Gastrointestinal: Mild transient diarrhea

Dermatological: Itching; transitory exanthema

Miscellaneous: Feeling of swelling of entire body

OVERDOSAGE: No overdosage has been reported with this drug.

DOSEAGE AND ADMINISTRATION: Avoid using the intravenous route. Use of this product intravenously will result in almost all of the vitamin being lost in the urine. Pernicious Anemia: Parenteral vitamin B₁₂ is the recommended treatment and will be required for the remainder of the patient’s life. The oral form is not dependable. A dose of 100 mcg daily for 6 or 7 days should be administered by intramuscular or deep subcutaneous injection. If there is clinical improvement and if a reticulocyte response is observed, the same amount may be given on alternate days for seven doses, then every 3 to 4 days for another 2 to 3 weeks. By this time hematologic values should have become normal. This regimen should be followed by 100 mcg monthly for life. Folic acid should be administered concomitantly if needed.

Patients with Normal Intestinal Absorption: Where the oral route is not deemed adequate, initial treatment similar to that for patients with pernicious anemia may be indicated depending on the severity of the deficiency. Chronic treatment should be with an oral B₁₂ preparation. If other vitamin deficiencies are present, they should be treated.