

Prescribing Information

VITAMIN B₁₂ (Cyanocobalamin injection USP)

HEMATOPOIETIC

PHARMACOLOGY

Vitamin B₁₂ is a group of cobalt-containing B complex vitamins, also known as cobalamins, synthesized by microorganisms. Cyanocobalamin and hydroxocobalamin are the principal forms of vitamin B₁₂ in clinical use. They have equivalent vitamin B₁₂ activity. An exogenous source of vitamin B₁₂ is required for nucleoprotein and myelin synthesis, cell production, normal growth, and for the maintenance of normal erythropoiesis.

Deficiency of vitamin B₁₂ may be caused by dietary deficiency, malabsorption, or lack of sufficient intrinsic factor, and results in megaloblastic anemia, gastrointestinal lesions and neurologic damage characterized by demyelination and progressive axonal degeneration. Therapy with vitamin B₁₂ reverses the anemia and gastrointestinal manifestations of deficiency, and halts the progression of neurologic damage. However, the existing nerve damage may not be completely reversible.

Pharmacokinetics: Vitamin B₁₂ is irregularly absorbed from the distal small intestine following oral administration. Vitamin B₁₂ absorption is an active process that requires gastric intrinsic factor. Intrinsic factor is a glycoprotein secreted by the gastric mucosa. Passive diffusion through the intestine wall can occur but large amounts of B₁₂ are required (i.e. > 1 mg). Following oral doses less than 3 µg, peak plasma concentrations are not reached for 8 to 12 hours because the vitamin is transiently retained in the wall of the lower ileum. It is rapidly absorbed from I.M. and S.C. sites of injection; peak plasma concentrations are reached within 1 hour after I.M. injection.

Vitamin B₁₂ is distributed into the liver, bone marrow, and other tissues, including the placenta. At birth, the serum concentration of vitamin B₁₂ in neonates is 3 to 5 times that of the mother.

Total body stores of vitamin B₁₂ in healthy individuals are estimated to range from 1 to 11 mg, with an average of 5 mg; 50 to 90% is stored in the liver. Vitamin B₁₂ is believed to be converted to coenzyme form in the liver and is probably stored in tissues in this form.

Following I.V. or I.M. administration of 0.1 to 1 mg of cyanocobalamin, 50 to 90% of the dose may be excreted in urine by glomerular filtration within 48 hours, with the major portion being excreted in the first 8 hours. Hydroxocobalamin is more highly protein bound and is retained in the body longer than cyanocobalamin; however, it is more effective in normalizing the hematocrit.

Because hydroxocobalamin may cause formation of antibodies to hydroxocobalamin-transcobalamin II complex, cyanocobalamin is usually the preferred form of vitamin B₁₂.

INDICATIONS

VITAMIN B₁₂ is used in the treatment of pernicious anemia and other vitamin B₁₂ deficiency states. Vitamin B₁₂ is also used to treat other macrocytic, megaloblastic anemias, in cases where malabsorption of vitamin B₁₂ is suspected, e.g., gastric carcinoma, gastrectomy, sprue, ileal resection, strictures, or anastomoses involving the ileum.

Vitamin B₁₂ deficiency requiring therapy may also be caused by lack of sufficient intrinsic factor which could have many causes, or by bacteria (blind loop syndrome), the fish tapeworm, or by certain drug therapies that may impair vitamin B₁₂ absorption (see **PRECAUTIONS, Drug Interactions**).

Vitamin B₁₂ is used in conjunction with radiolabelled vitamin B₁₂ in the study of vitamin B₁₂ absorption and diagnosis of pernicious anemia (Schilling test).

CONTRAINDICATIONS

Hypersensitivity to cobalamins.

PRECAUTIONS

An intradermal sensitivity test may be performed in patients with suspected hypersensitivity to cobalamins.

In the treatment of megaloblastic anemia, erythrocyte potassium requirements may be increased as erythropoiesis normalizes, and potassium administration may be required.

It is important to accurately diagnose anemias prior to treatment, to ensure the proper therapy is initiated. If folic acid is used to treat pernicious anemia, for example, hematologic improvement may occur while neurologic complications continue to progress.

Cyanocobalamin (specifically) has been associated with accelerated optic nerve atrophy in patients with early Leber's disease (hereditary optic nerve atrophy) and its use should be avoided in these patients.

Drug Interactions: Most antibiotics, methotrexate and pyrimethamine invalidate folic acid and vitamin B₁₂ diagnostic microbiological blood assays. Chloramphenicol may antagonize the hematopoietic response to vitamin B₁₂.

Colchicine, aminoglycosides, certain anticonvulsants (e.g. phenytoin, phenobarbital, primidone), para-aminosalicylic acid or excessive alcohol intake for longer than 2 weeks may impair the absorption of vitamin B₁₂.

Histamine₂-Receptor Antagonists (cimetidine, ranitidine, nizatidine, famotidine): May potentially cause vitamin B₁₂ deficiency by decreasing gastric acid cleavage of vitamin

B₁₂ from food sources. This may be important in patients with low stores of vitamin B₁₂ or in patients taking H₂-antagonists for extended periods of time (> 2 years).

Pregnancy: No adverse effects have been reported with ingestion of normal daily requirements during pregnancy.

Lactation: Vitamin B₁₂ is distributed into the milk of nursing women in concentrations that approximate the maternal blood vitamin B₁₂ concentration. No adverse effects have been reported with intake of normal daily requirements during lactation.

ADVERSE EFFECTS

Vitamin B₁₂ is usually non-toxic even in large doses. However, some adverse effects have been reported such as mild, transient diarrhea, itch, urticaria.

DOSAGE

In the prevention of deficiency of any nutrient, adequate dietary intake is preferred over supplementation whenever possible. Vitamin B₁₂ is found in liver, meat, dairy foods, fish and shellfish.

The preferred route of administration of vitamin B₁₂ is parenteral, either I.M. or deep S.C. (Avoiding the dermis and upper subcutaneous tissue). The preferred form of vitamin B₁₂ is cyanocobalamin (see **PHARMACOLOGY**).

Treatment of vitamin B₁₂ Deficiency: Confirmatory diagnostic tests should be performed prior to initiation of therapy.

Adults: The usual I.M. or S.C. dose is 30 to 100 µg daily for 5 to 10 days. A maintenance dose of 100 to 200 µg monthly is usually sufficient to maintain normal erythrocyte count. Although the oral route is generally considered to be inferior to parenteral therapy in the treatment of vitamin B₁₂ deficiencies, oral dosages of up to 1000 µg daily have been used in patients who have refused parenteral therapy.

Children: 100 µg I.M. or S.C. daily until a total dose of 1 to 5 mg is given. The maintenance dose is 60 µg monthly.

It is important that patients understand their need for lifelong, regular maintenance therapy.

AVAILABILITY OF DOSAGE FORM

Each mL contains: Cyanocobalamin 1000 µg, benzyl alcohol 1.5%, sodium chloride 8 mg, sodium phosphate monobasic monohydrate 2.3 mg, hydrochloric acid and/or sodium hydroxide (for pH adjustment) in water for injection.

Omega

Montreal, Quebec H3M 3A2

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