

Vitamin B12

Cyanocobalamin

100 mcg Tablets



Product Summary:

Water-soluble vitamin that helps the body metabolize carbohydrates, fats and proteins, form red blood cells, and prevent vitamin B12 deficiency. Other uses of vitamin B12 for overall health include depression diabetic neuropathy, impaired mental function in the elderly, low sperm count, multiple sclerosis, tinnitus, and reducing elevated plasma homocysteine levels along with folic acid.

Properties/Uses:

The claim approved by *Natural Health Products Directorate* (NHPD): A factor in the maintenance of good health. Helps the body metabolize fats, proteins and carbohydrates. Helps form red blood cells.



BLOOD





Pharmacology:

Vitamin B12 is the common name of cobalamin (a tetrapyrrole structure that chelates an atom of cobalt in the center of the structure). Cobalamin is synthesized only by animal gut bacteria, but is distributed throughout all forms of animal tissue, with the liver being the site of highest concentration. The active forms in the body include methylcobalamin and deoxyadenosylcobalamin, both essential cofactors for two enzymes of intracellular metabolism. The methyl form attaches to *methionine synthase* and the adenosyl form attaches to *methymalonyl CoA mutase*.¹ *Methionine synthase* mediates two crucial intracellular metabolic processes: the synthesis of nucleic acid (controls growth and cellular division) and numerous methylation reactions. *Methymalonyl CoA mutase* facilitates the conversion of propionic acid to succinic acid, which is essential to fatty acid metabolism.¹ Deficiency of cobalamin leads to two well recognized clinical manifestations:^{1,2}

1. Pernicious anemia or megaloblastic anemia, because the red blood cells are larger than normal.
2. Cobalamin-associated neuropathy in which the spinal cord, brain, optic nerve and peripheral nerves may be affected.

Vitamin B12 is found mostly in animal products, and is required for fat and carbohydrate metabolism, and protein synthesis. Along with folic acid, vitamin B12 reduces levels of homocysteine, a risk factor for cardiovascular disease. It is important in the treatment of pernicious anemia and is part of the coenzyme responsible for new cell synthesis, maintaining nerve cells, and breaking down amino acids and some fatty acids.^{3,4}

Vitamin B12 and Hyperhomocysteinemia

An important manifestation of vitamin B12 deficiency, and the failed methylation that vitamin B12 deficiency brings, is the elevation of plasma homocysteine. Elevated plasma homocysteine is now viewed by many experts as a greater risk factor than elevated cholesterol for developing coronary heart disease.⁵ Homocysteine must be methylated to form methionine via vitamin B12 or folic acid, or converted to cysteine via vitamin B6. Homocysteine is a natural cellular by-product of methionine metabolism, intended to have a transient existence. Failure to metabolize homocysteine to methionine or cysteine leads to unresolved elevated plasma levels. Homocysteine is cytotoxic to the endothelium and is able to initiate the focal lesions that will become coronary atherosclerosis.⁵

Many studies have indicated an association between homocysteine and diabetic retinopathy. A cross-sectional case-control study was conducted with 100 normal control subjects and 300 subjects with type-2 diabetes.⁶ Of the 300 subjects with type 2 diabetes, 200 had diabetic retinopathy and 100 did not. While mean plasma homocysteine levels were found to be higher in type 2 diabetic patients compared with the control subjects, homocysteine levels were particularly high in the diabetic



retinopathy group. In addition, plasma vitamin B12 levels were found to be significantly lower in the diabetes groups compared with the control group. Higher homocysteine levels were significantly associated with lower vitamin B12 and folic acid but not with other B-vitamins. Additionally, hyperhomocysteinemia and vitamin B12 deficiency did not seem to be related to subjects' age, body mass index, or duration of diabetes. These results thus suggest a possible association between vitamin B12 deficiency and hyperhomocysteinemia in diabetic retinopathy.

Vitamin B12 and the Aging Population

Absorption of vitamin B12 may be diminished simply as a result of growing older, even when some measure of gastric intrinsic factor is present.⁵ This is likely to be an important reason in explaining why a significant number of the elderly have demonstrated lower plasma B12 levels. Impaired neurological function in the elder population due to vitamin B12 depletion can be an important but unsuspected factor when there is not also evidence of anemia. Many physicians fail to investigate vitamin B12 depletion if there is not also evidence of anemia, yet two of the most depleted nutrients in the elder population are vitamin B12 and folic acid.⁷ In all cases of impaired mental function or depression vitamin B12 status should be determined and treated accordingly.^{8,9} Older patients at the pharmacy should be encouraged to have their physician assess their B12 status.

In a recent cross-sectional examination, concentrations of vitamin B12-related markers were associated with global cognitive function and with total brain volume.¹⁰ The study involved 121 older residents of the south side of Chicago who were part of the Chicago Health and Aging Project (CHAP). The participants had blood drawn to measure levels of vitamin B12 and B12-related markers that can indicate a B12 deficiency. The same subjects took tests measuring their memory and other cognitive skills. MRI scans of the participants' brains were taken about four-and-a-half years later to measure total brain volume and to look for other signs of brain damage. The researchers found that having high levels of four of five markers for vitamin B12 deficiency was associated with having lower scores on the cognitive tests and smaller total brain volume. Specifically, methylmalonate levels were associated with poorer episodic memory and perceptual speed, and homocysteine concentrations were associated with decreased total brain volume.

The relation between serum levels of homocysteine and holotranscobalamin (the active portion of the vitamin B12), and the risk of incident Alzheimer disease (AD) was studied in a sample of Finnish community-dwelling elderly.¹¹ A dementia-free sample of 271 subjects aged 65–79 years derived from the Cardiovascular Risk Factors, Aging, and Dementia (CAIDE) study was followed up for 7 years to detect incident AD. The study found that for each micromolar increase in the concentration of homocysteine, the risk of Alzheimer's disease increased by 16 percent, whereas each picomolar increase in concentration of the active form of vitamin B12 reduced risk by two percent. The results stayed the same after taking into account other factors, such as age, gender,





education, smoking status, blood pressure and body mass index. The addition of folate did not appear to raise or lower the risk of Alzheimer's disease.

Drug-Induced Nutrient Depletion of Vitamin B12

Commonly prescribed drugs are known to cause nutrient deficiencies. As noted in the *Interactions* section, vitamin B12 may be depleted by a number of medications such as metformin and proton pump inhibitors.

Since 1970, annual measurement of serum vitamin B12 levels has been recommended for patients on long term metformin therapy.¹² Vitamin B12 malabsorption was found to be 30% in patients taking long-term metformin therapy, and low serum levels of vitamin B12 were found in approximately 20% of patients having vitamin B12 malabsorption.¹² Metformin inhibits active vitamin B12 absorption in the distal ileum,¹³ by affecting calcium-dependent membrane action. Cross-sectional studies indicate significant depletion of vitamin B12 with long-term use of metformin.^{14,15,16,17} One long-term multicentre randomized placebo controlled trial (n=390) studied the effects of metformin treatment (850 mg three times per day for 4.3 years) on serum concentrations of vitamins B12, folate and homocysteine in type 2 diabetes patients. Metformin was associated with decreased vitamin B12 concentrations by 19% (p<0.001), decreased folate concentration by 5% (p=0.033) and increased homocysteine concentration by 5% (p=0.091).¹⁸

Mild B12 deficiency has been demonstrated in at least 1/4 of patients on long-term proton pump inhibitors.¹⁹ Reduced secretion of gastric acid and pepsin produced by proton pump inhibitors may reduce absorption of protein-bound (dietary) vitamin B12.^{19,20,21} Prolonged treatment can significantly decrease serum B12 levels and cause vitamin B12 deficiency in some patients.^{22,23} However, in one study, omeprazole reduced absorption of protein-bound, but not unbound, cyanocobalamin; no change in serum cobalamin was observed in patients after 7 years of treatment.²⁴ Given the uncertainty of the depletion of serum vitamin B12 levels, periodic monitoring of B12, methylmalonic acid and homocysteine may be useful in patients.¹⁹



Manufactured product information:

Manufacturer:

WN Pharmaceuticals® Ltd.

Size/UPC:

100's 7 77747 10314 0

NPN:

80004461

Expiry Date:

36 months from date of manufacture

Active Ingredient:

Each tablet contains:

Vitamin B12 (Cyanocobalamin) 100 mcg

Non-Medicinal Ingredients (in descending order):

Microcrystalline cellulose, magnesium stearate

Appearance:

Light pink lightly speckled round uncoated tablet.

Packaging:

175 cc white round bottle with safety seal under a 38 mm white induction sealed cap with vented interior seal and a label applied to the bottle. Lot number and expiry date are printed on the label applied to the exterior of the bottle.

Storage:

Keep at room temperature in a dark, dry place.





Dose:

The recommended dosage to correct nutritional deficiency of vitamin B12 is 25 to 250 mcg per day.²⁵ Oral doses between 500 to 1000 mcg per day have been recommended for the treatment of pernicious anemia.²⁶

Directions:

(Adults): 1 tablet, 1 – 4 times daily or as recommended by a physician.

Caution:

The caution as approved by the *Natural Health Products Directorate* (NHPD): KEEP OUT OF THE REACH OF CHILDREN. STORE AT ROOM TEMPERATURE IN A DARK, DRY PLACE. DO NOT USE IF SEAL UNDER CAP IS BROKEN OR MISSING.

Deficiency Symptoms:

Symptoms of vitamin B12 deficiency are rare, taking years to develop complications associated with long-term depletion of this nutrient.^{27,28} Deficiency of vitamin B12 may lead to anemia, progressive nerve damage, and sore tongue.³ Prolonged deficiency can lead to pernicious or megaloblastic anemia and hyperhomocysteinemia.^{12,29} Other documented deficiency symptoms include irritability, weakness, numbness, myelopathy, fatigue, glossitis, anorexia, nausea, vomiting, glossitis, dermatitis, headache, palpitations, and altered mental status, including personality and behavioral changes (confusion, depression, psychosis).^{4,25} Low vitamin B12 levels may increase the risk of colon cancer, heart disease, brain dysfunction, birth defects and irreversible neuropathy.^{25,30}

Drug Interactions/Contraindications

*Drug Interactions:*³¹

Anti-inflammatory Medications:

Inhalant, Systemic, and Topical Corticosteroids: Beclomethasone, Budesonide, Dexamethasone, Fluticasone, Hydrocortisone, Methylprednisolone, Mometasone Furoate, Prednisone, Triamcinolone



Antibiotic Medications:

Aminoglycosides: Gentamicin, Neomycin, Tobramycin

Antibiotic Combination: Sulfa Drugs: Co-Trimoxazole, Trimethoprim, Trimethoprim-Sulfamethoxazole

Cephalosporins: Cefprozil, Cefuroxime, Loracarbef

Macrolides: Azithromycin, Clarithromycin, Erythromycin

Penicillin Derivatives: Amoxicillin, Amoxicillin and Clavulanate, Penicillin V Potassium

Quinolones: Cinoxacin, Ciprofloxacin, Enoxacin, Gatifloxacin, Levofloxacin, Lomefloxacin, Moxifloxacin, Nalidixic Acid, Norfloxacin, Ofloxacin, Sparfloxacin, Trovafloxacin

Tetracycline Derivatives: Doxycycline, Minocycline, Tetracycline

Anticonvulsant Medications:

Barbiturates: Phenobarbital

Antidiabetic Medications:

Biguanides: Metformin

Birth Control Medications:

Monophasic, Biphasic, and Triphasic Preparations

Cardiovascular Medications:

Electrolytes

Cholesterol-Lowering Medications:

Bile Acid Sequestrants: Cholestyramine, Colestipol

Gout Medications:

Uricosuric Agents: Colchicine

Ulcer Medications:

Histamine H2 Antagonists: Cimetidine, Famotidine, Nizatidine, Ranitidine Bismuth Citrate, Ranitidine Hydrochloride

Proton Pump Inhibitors (Gastric Acid Secretion Inhibitors): Lansoprazole, Omeprazole

Nutrient Interactions:⁷ Vitamin B12, folic acid, and vitamin B6 have a recognized interactive relationship.





Toxicity/Adverse Reactions:

The body is able to achieve high blood and tissue levels of vitamin B12 without toxicity.^{4,7} Infrequent diarrhea, itching, rash, transitory exanthema, and urticaria have been reported.





Allergen Content/Ingredient Sensitivity:

NO	YES
Artificial Colors	
Artificial Flavors	
Artificial Sweeteners	
Corn Products	
Egg Products	
Fish	
Gluten	
Hydrolyzed Plant Protein	
Lecithin	
Milk Products	
Peanuts	
Preservatives	
Sesame Products	
Shellfish	
Soy Products	
Starch/Modified Starch	
Sulphites	
Tartrazine	
Tree Nuts	
Wheat Products	
Yeast	

ACCEPTABLE FOR THE FOLLOWING DIETARY RESTRICTION:

Free of animal products

NOT ACCEPTABLE FOR THE FOLLOWING DIETARY RESTRICTION:

Kosher





References:

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