For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

Cobasoft OD

(Mecobalamin, Alpha Lipoic Acid, Folic Acid & Pyridoxine Hydrochloride Capsules)

COMPOSITION

Each soft gelatin capsule contains:

Mecobalamin J.P. 1.5mg

Alpha Lipoic acid U.S.P. 100mg

Folic Acid I.P. 1.5mg

Pyridoxine Hydrochloride I.P. 3.0 mg

Colour: Ponceau 4R and Titanium Dioxide I.P.

Appropriate overages added

DESCRIPTION

Mecobalamin is one of the two active coenzyme form of vitamin B12. Its chemical name is a-(5,6-Dimethylbenzimidazolyl)-Co-methyl-cobamide. It has a molecular weight of 1344.40. The molecular formula is $C_{63}H_{91}CON_{13}O_{14}P$.

Alpha-lipoic acid is a disulfide compound that is a cofactor in vital energy producing reactions in the body. It is also known as thioctic acid. Its chemical name is 5-[1,2-dithiolan-3-yl)]-valeric acid. It has a molecular weight of 206.3 and the molecular formula is $C_8H_{14}O_2S_2$.

Folic acid is also known as pteroylmonoglutamic acid. Its chemical name is N-[4- (2-amino-4 hydroxy pteridin-6yl-methylamino)benzoyl]-L (+)-glutamic acid. Its molecular weight is 441.40 and its molecular formula is $C_{19}H_{19}N_7O_6$.

Pyridoxine hydrochloride is the principle form of vitamin B6 used in nutritional supplements. Its chemical name is 5-hydroxy-6-methylpyridine-3,4-dimenthanol hydrochloride. Its

molecular weight is 205.6 and its molecular formula is $C_8H_{11}NO_3HCl$.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Mecobalamin

Mecobalamin is involved in the synthesis of thymidine from deoxyuridine and promotes the synthesis of DNA and RNA by acting as a coenzyme in the formation of methionine from homocysteine. It enhances synthesis of lecithin, a major component of myelin sheath. Mecobalamin is known to be extensively taken up by the nerve cell organelles than cyanocobalamin in animals. It is also reported to maintain axonal function by promoting nucleic acid and protein synthesis.

Mecobalamin has been demonstrated by neuropathological and electrophysiological studies to inhibit nerve fibre degeneration in neuropathies (in rats and rabbits) induced by drugs, such as adriamycin, acrylamide and vincrinstine or with streptozocin-induced diabetes. Mecobalamin is also reported to be as effective as steroids in accelerating the recovery of injured nerve tissues from paralysis.

Mecobalamin is reported to accelerate the synthesis of nucleic acids in bone marrow, as well as the maturation and division of erythroblasts, resulting in an increase in the production of erythrocytes.

Alpha lipoic acid

Alpha lipoic acid has biological antioxidant activity, antioxidant recycling activity and activity in enhancing biological energy production.

Alpha lipoic acid and its reduced metabolite, dihydrolipoic acid (DHLA), are reported to form a redox couple and scavenge a wide range of reactive oxygen species.

Alpha lipoic acid appears to participate in the recycling of other important biological antioxidants, such as vitamin E and C, ubiquinone and glutathione.

Alpha lipoic acid increases glucose uptake through recruitment of the glucose transporter-4 to

plasma membranes, a mechanism that is shared with insulin stimulated glucose uptake.

Folic acid

Folic acid lowers the risk of neural tube defects. It is also reported to have antiatherogenic, anticarcinogenic, neuroprotective and antidepressant actions.

Folic acid lowers homocysteine by converting homocysteine to methionine. A high intake of folate has been associated with a lower risk of coronary events.

Folic acid and 5-methyltetrahydrofolate have been demonstrated to restore impaired Nitric oxide (NO) status in hypercholesterolemic subjects. In cultured endothelial cells, 5-methyltetrahydrofolate was found to enhance the enzymatic activity of partially tetrahydrobiopterin (BH4)-repleted endothelial nitric oxide synthase (eNOS), enhancing NO formation. The enhancement of eNOS activity may be another mechanism for the possible antiatherogenic activity of folic acid.

5-Methyltetrahydrofolate has been found to directly scavenge superoxide radicals in vitro. Activated eNOS also decreases the production of superoxide. Uncoupling of eNOS, which occurs under conditions of hypercholesterolemia, results in decreased production of NO and increased production of superoxide. Folate appears to restore impaired NO availability by an ameliorative effect on eNOS uncoupling.

Pyridoxine

Pyridoxine is essential for normal brain development and function and participates in the process of synthesizing neurotransmitters.

Pyridoxine is especially important vitamin for maintaining healthy nerve and muscle cells and it aids in the production of DNA and RNA.

Pyridoxine is considered an antistress vitamin because it is believed to enhance the activity of the immune system.

Pyridoxine with mecobalamin and folic acid work together to control blood levels of homocysteine. Hyperhomocysteinemia is an independent risk factor for atherosclerosis and

coronary heart disease.

Pharmacokinetics

Mecobalamin is utilized more efficiently than cyanocobalamin to increase the levels of coenzyme forms of vitamin B12. The peak plasma concentration (Cmax) with a single oral dose of mecobalamin 1500 μ g in healthy individuals, is reported to be 972 – 55, 255 – 51, 36.0 – 7.9 pg/mL and is achieved in 3.6 – 0.5 hours. 40 to 80 percent of the cumulative amount of total mecobalamin is excreted in the urine within the first 8 hrs. The half life ($t_{1/2}$) is reported as 12.5 hours.

Alpha lipoic acid is rapidly absorbed after oral administration, as indicated by the Tmax of about 0.8 hours, with a limited oral bioavailability due to a high first pass metabolism. In healthy volunteers, a mean bioavailability of 29.1 – 10.3 % was reported following single oral administration of 200 mg tablet. The bioavailability diminished significantly when administered with food. The terminal phase elimination half life ($t_{1/2}$) was reported as 0.5 hours.

Folic acid is rapidly absorbed from the proximal part of the intestine (duodenum and jejunum). Folic acid administered therapeutically enters the portal circulation largely unchanged since it is a poor substrate for reduction by dihydrofolate reductase. It is converted to the metabolically active form 5- methyltetrahydrofolate in the plasma and liver. Folate undergoes enterohepatic circulation. Folate metabolites are eliminated in the urine and folate in excess of body requirements is excreted unchanged in the urine. Folate is distributed into breast milk.

Pyridoxine is readily absorbed from the gastrointestinal tract, converted to the active forms and stored in the liver and brain. It is metabolized in the liver and excreted in the urine. Pyridoxine crosses the placenta and is excreted in breast milk.

INDICATIONS AND USAGE

For the treatment of diabetic neuropathy

CONTRAINDICATIONS

Cobasoft OD is contraindicated in those hypersensitive to any constituent of the product.

WARNINGS

The use of Cobasoft OD to treat any medical condition requires medical supervision.

Cobasoft OD should not be used over a period of months if there is lack of satisfactory clinical response in patients with diabetic neuropathies.

Because of lack of long term safety data of alpha-lipoic acid, Cobasoft OD should be avoided in pregnant women and nursing mothers.

PRECAUTIONS

Alpha lipoic acid:

Patients with diabetes and problems with glucose intolerance should be cautioned that supplemental alpha-lipoic acid may lower blood glucose levels. Blood glucose should be monitored and antidiabetic drug dose adjusted, if necessary, to avoid possible hypoglycemia.

Pyridoxine: Those who are being treated with levodopa without concurrently taking carbidopa should avoid doses of pyridoxine of 5 mg or greater daily.

ADVERSE REACTIONS

Constituents in Cobasoft OD are generally well tolerated.

DOSAGE AND ADMINISTRATION

One capsule of Cobasoft OD to be taken daily.

Expiry date

Do not use later than the date of expiry.

Storage

Store in a cool dry and dark place below 25°C

Presentation

Cobasoft OD is available as blister strip of 10 capsules

MARKETED BY:

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