Thiamine Mononitrate
Pyridoxine HCl
Cyanocobalamin
Folic Acid

Meganerv ™ F•A

100 mg/50 mg/2.5 mg/1.2 mg Tablet

Vitamins

FORMULATION:
Each tablet contains:
Thiamine Mononitrate (Vitamin B1) ..... 100 mg
Pyridoxine HCl (Vitamin B6) ..... 50 mg
Cyanocobalamin (Vitamin B12) ..... 1.2 mg
Folic Acid ..... 2.5 mg

DESCRIPTION:
Meganerv™ F•A is a brown, round, film-coated tablet and plain on both sides.

PHARMACODYNAMICS AND PHARMACOKINETICS:
Thiamine (Vitamin B1) functions as a coenzyme of carbohydrate metabolism. It is specifically involved in the decarboxylation of alpha-ketoacids such as pyruvate and alpha-ketoglutarate, and utilization of pentose in the hexose monophosphate shunt. Without thiamine, pyruvic acid cannot be further bio-transformed into the active form which is utilized to produce the energy needed for cellular activities. Impaired oxidation of the alpha-ketoacids leads to the accumulation of metabolites of the reaction, which are toxic to the cells of the central nervous system (CNS). Thiamine therefore ensures the efficient metabolism of glucose and the conversion of glucose into ribose, a major component of DNA and RNA. Thiamine activates production of energy from glucose and storage of energy as fat, making energy available to support normal cellular processes.

Thiamine is especially needed for the normal functions of the gastrointestinal, cardiovascular and nervous systems of the body. The muscle cells of the heart, blood vessels and the secretory glands of the gastrointestinal tract depend on the energy derived from the metabolism of glucose, which thiamine catalyzes. A lack of thiamine leads to weakness in these muscles. The cells of the CNS also depend exclusively on glucose as its source of energy. When there is thiamine deficiency, glucose utilization by nervous tissue decreases markedly and the communication in many different portions of the CNS is disrupted. Independent of its coenzyme function, thiamine also acts as a modulator in the transmission of neural impulses. Thiamine deficiency can cause degeneration of myelin sheaths in the peripheral nerves and in the CNS. This can lead to polyneuritis, a condition characterized by radiating pain along the course of one or more peripheral nerves.

Thiamine (Vitamin B1) is absorbed after oral administration mainly in the duodenum and is widely distributed to most body tissues. Thiamine may appear in breast milk. Excess amounts are excreted unchanged in the urine.

Pyridoxine (Vitamin B6) participates in many cellular reactions of lipid and amino acid metabolism. The active form of B6, pyridoxal phosphate, acts as a coenzyme in several metabolic transformations of amino acids, which are in turn needed for tissue building and repair and the synthesis of blood elements and certain compounds like neurotransmitters. Pyridoxine is required in the synthesis of delta-aminolevulinic acid, the precursor of heme, necessary for the formation of the hemoglobin molecule. Pyridoxine is therefore essential for proper synthesis of red blood cells. Pyridoxine is also of particular importance in the synthesis of neurotransmitters, which are required for the normal activity of the brain and the entire

CNS. A deficiency of pyridoxine causes abnormal CNS function, hyperirritability, neuritis and even convulsions.

A large portion of the body's pyridoxine is found in phosphorylase (approximately half is found in skeletal phosphorylase), the enzyme that converts glycogen to glucose-1-phosphate and the carbohydrate form that can be used for energy.

After oral administration, pyridoxine (Vitamin B6) is rapidly absorbed from the gastrointestinal tract and is converted to pyridoxal phosphate which is the active form. Storage is primarily in the liver and amount in excess of the body's requirements are excreted unchanged in the urine.

Meganerv™ F•A contains high amounts of cyanocobalamin (Vitamin B12), a coenzyme involved in several metabolic pathways. Among the important actions of cyanocobalamin is to act as a coenzyme of nucleic acid metabolism reducing ribonucleotides to deoxyribonucleotides, a step that is essential in the replication of genes and formation of new cells and the conversion of methylmalonyl-CoA to succinyl CoA. Cyanocobalamin is also an important cofactor in the formation and maturation of red blood cells in the bone marrow. Deficiency of cyanocobalamin results in megaloblastic anemia.

Cyanocobalamin is also involved in the formation of myelin sheaths in nervous tissue. A deficiency causes demyelination of the large nerve fibers of the spinal cord. The inhibition of normal fatty acid synthesis in the brain and nerve tissues leads to faulty structure and impaired functions manifested as neurological symptoms.

Cyanocobalamin (Vitamin B12) is absorbed from the gastrointestinal tract and is extensively bound to plasma protein (transcobalamin) which is responsible for the rapid transport of the cobalamins to tissues. Cyanocobalamin may appear in breast milk and diffuses across placenta. Cyanocobalamin is stored in the liver and is excreted in the bile.

Folic acid, in its reduced form tetrahydrofolate, participates in many reactions involving one-carbon transfers. It is involved in the conversion of homocysteine to methionine and in the conversion of deoxyuridylate to thymidylate, an essential step required in the synthesis of DNA.

Folic acid is necessary for the normal production of red blood cells, including maturation of megaloblasts into normoblast.

After oral administration, folic acid is rapidly absorbed from the gastrointestinal tract, mainly from the duodenum and jejunum. Folic acid is converted to its active form, 5-methyltetrahydrofolate, in the plasma and liver. Storage is primarily in the liver and is also actively concentrated in the cerebrospinal fluid. Amounts in excess of the body's requirements are excreted unchanged in the urine.

INDICATIONS:

- Painful neurological manifestations such as neuritis, polyneuritis, neuralgia, lumbago, ischialgia, sciatica, and cervical and shoulder arm syndrome.
- Neuropathies associated with certain disease states such as diabetes mellitus and cardiac disorders; alcoholic neuropathy; iatrogenic complications arising from isoniazid (INH), reserpine, and phenothiazine therapy; other drug induced neuropathies, neuropathic changes during pregnancy, and hyperemesis gravidarum.
- Prophylaxis and treatment of nutritional megaloblastic anemia associated with folic acid deficiency, as in hemolytic anemia, pernicious anemia, alcoholism, and that following gastrectomy.
- Prevention of neural tube defects.
- As adjunct in the treatment of colorectal carcinoma, ulcerative colitis, sickle cell diseases and homocysteinemia.
- To correct decreased folate levels when taking the following: methotrexate, trimethoprim, sulfamethoxazole, phenytoin and oral contraceptive pills.

DOSAGE AND ADMINISTRATION:

For therapeutic use, 2-4 tablets should be administered daily. Chronic cases that may require longer therapy must be under constant physician supervision. For prophylactic use when

diseases or drugs are likely to lead to neurological complications, 1-2 tablets daily are recommended.

For prophylaxis and treatment of anemia associated with folic acid deficiency, one tablet daily.

For the prevention of neural tube defects in women at high risk, 1-4 tablets daily taken at least one month before conception through the first trimester of pregnancy.

Or as prescribed by the physician.

CONTRAINDICATIONS/PRECAUTIONS/WARNINGS:
Folic acid should not be used in the therapy of patients with vitamin B12 deficiency of any cause unless there is associated folate deficiency. Proper hematological diagnosis is essential. The folic acid content of one tablet a day however, is unlikely to mask pernicious anemia should this condition be present. There are no known contraindications to the other components of Meganerv™ F•A, as used in this formulation.

Folic acid should never be given alone or with inadequate amounts of vitamin B12 for the treatment of undiagnosed megaloblastic anemia.

PREGNANCY AND LACTATION:
Vitamin B1, B6 and B12 can be given safely for pregnant and lactating women.

Although folic acid is excreted into breast milk, no adverse effects have been observed in breastfeeding infants whose mothers were receiving folic acid. Though some have expressed concern over inhibition of breast milk secretion by pyridoxine, others have cautioned that pyridoxine deficiency may cause seizures in the neonate.

ADVERSE DRUG REACTIONS:
Adverse effects seldom occur after oral administration of thiamine and cyanocobalamin, but hypersensitivity reactions have been reported after parenteral administration. Hypersensitivity reactions to thiamine ranged from very mild to very rarely, anaphylactic shock. Hypersensitivity reactions have occurred rarely following parenteral administration of cyanocobalamin.

Folic acid is generally safe and well tolerated. Adverse reactions including gastrointestinal disturbances and hypersensitivity have been reported rarely.

DRUG INTERACTIONS:
Pyridoxine reduces the effects of levodopa. It has also been reported to decrease the serum concentrations of phenobarbital and phenytoin.

Drugs that increase the requirements for pyridoxine include hydralazine, isoniazid, penicillamine, and oral contraceptives.

Drugs that may reduce the absorption of cyanocobalamin from gastrointestinal tract include neomycin, aminosalicylic acid, histamine-2 receptor antagonists, and colchicine.

Oral contraceptives may reduce serum concentrations of vitamin, B12. Though unlikely to be of clinical significance, many interactions of vitamin B12 should be taken into account when performing assays for blood concentration.

OVERDOSAGE AND TREATMENT:
The formulation consists of vitamins B1, B6, B9 and B12 which are all water-soluble. Any excess intake will be readily eliminated in the urine. The formulation is therefore safe for long-term use. Folic acid is usually well tolerated in prescribed dosage. Folic acid may partially reverse the anti-epileptic effects of phenobarbital, diphenylhydantoin, and primidone, and may thereby increase seizure frequency. The combination of folic acid and vitamin B12 makes it safe to use in the treatment of pernicious anemia. Sensitivity to vitamin B1 may occur if administration is at prolonged intervals, is irregular, or if the initial dose is low and is suddenly increased. Liver dysfunction also seems to predispose patients to hypersensitivity reactions. Nevertheless, it must be stressed that hypersensitivity to vitamin B1 is very rare when given orally and is encountered more often only when given by intravenous injection.

In cases of oral overdose, appropriate medical management should be done as recommended by the National Poison center.

AVAILABILITY:
Strip foil x 4's (Box of 100's)

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibit dispensing without prescription.

DR-XY30034

STORE AT TEMPERATURES NOT EXCEEDING 30°C.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph

SVMore

Manufactured for:
S.V. MORE PHARMA CORPORATION
5th Flr., S.V. More Group Corporate Center
#16 Scout Tuazon cor. Roces Ave.,Quezon City
Metro Manila, Philippines
by: Hizon Laboratories, Inc.
Assumption Road, Sumulong Highway,
Antipolo City

Date of Renewal of Authorization: 22 September 2019
Date of Revision of Package Insert: 17 June 2019