

PYFOMIN

Tablets

پایفومین
ٹیبلیٹس

(L-Methylfolate Calcium+Pyridoxal-5'-Phosphate+
Methylcobalamin)

(L-میتھیل فولیٹ کالسیئم + پیریدوکسال-5'-فوسفیت +
میتھیل کوبالامین ٹیبلیٹس)

DESCRIPTION: Pyfomin is used as a nutritional product for the clinical dietary management of endothelial dysfunction associated with diabetic peripheral neuropathy.

COMPOSITION:

Each film coated tablet contains:
L-Methylfolate Calcium 3mg
Pyridoxal - 5' - Phosphate ... 35mg
Methylcobalamin 2mg
Manufacturer's Specs.

INDICATION AND USAGE:

Pyfomin tablets are recommended for the patients with loss of protective sensation and neuropathic pain associated with diabetic peripheral neuropathy.

DOSAGE:

The recommended dose is one tablet twice daily or as directed by the healthcare professional. Pyfomin should always be used under medical supervision.

CLINICAL PHARMACOLOGY: L-methylfolate or 6(S)-5-methyltetrahydrofolate [6(S)-5-MTHF], is the primary biologically active diastereoisomer of folate and the primary form of folate in circulation. It is also the form which is transported across membranes into peripheral tissues, particularly across the blood brain barrier. In the cell, 6(S)-5-MTHF is used in the methylation of homocysteine to form methionine and tetrahydrofolate (THF). THF is the immediate acceptor of one carbon units for the synthesis of thymidine-DNA, purines (RNA and DNA) and methionine. About 70% of food folate and cellular folate is comprised of 6(S)-5-MTHF. Folic acid, the synthetic form of folate, must undergo enzymatic reduction by methylenetetrahydrofolate reductase (MTHFR) to become biologically active. Genetic mutations of MTHFR result in a cell's inability to convert folic acid to 6(S)-5-MTHF. L-methylfolate is a substantially diastereoisomerically pure source of L-methylfolate containing not more than 1% D-methylfolate which results in not more than 0.03 milligrams of D-methylfolate in Pyfomin. Pyridoxal-5-phosphate (P5P) is the active form of vitamin B6 and is used as the prosthetic group for many of the enzymes where this vitamin is involved, P5P is readily absorbed by the intestine by a process which is preceded by dephosphorylation to form pyridoxal. The phosphate group is regained during passage through the intestine. Pyridoxine, the parent compound of P5P and the most frequently used form of vitamin B6, requires reduction and phosphorylation before becoming biologically active. The P5P in Pyfomin contains 25mg of pyridoxal (the active component of P5P). Methylcobalamin (Methyl-B12) is one of the two forms of biologically active vitamin B12. Methyl-B12 is the principal form of circulating vitamin B12, hence the form which is transported into peripheral tissue. Methyl-B12 is absorbed by the intestine by a specific mechanism which uses the intrinsic factor and by a diffusion process in which approximately 1% of the ingested dose is absorbed. Cyanocobalamin and hydroxycobalamin are forms of the vitamin that require conversion to methylcobalamin.

PHARMACOKINETICS:

Absorption: In a study of subjects with coronary artery disease (n=21), peak plasma levels were reached in 1-3 hours following oral/parenteral administration. Peak concentrations of L-methylfolate were found to be more than seven times higher than folic acid (129 ng ml⁻¹ vs. 14.1 ng ml⁻¹) following oral/parenteral administration. The mean values for C_{max}, T_{max}, and AUC 0-12 were 129 ng ml⁻¹ 1.3 hours, and 363 respectively. After oral administration, Pyridoxal-5-Phosphate and its substituents absorbed readily from GI tract. Normal serum levels are 30 to 80ng/ml. Methylcobalamin substances bind to intrinsic factor, a glycoprotein secreted by the gastric mucosa, and are then actively absorbed from the gastrointestinal tract. Absorption is impaired in patients with an absence of intrinsic factor, with a malabsorption syndrome or with disease or abnormality of the gut, or after gastrectomy. Absorption from the gastrointestinal tract can also occur by passive diffusion; little of the vitamin present in food is absorbed in this manner although the process becomes increasingly important with larger amounts such as those used therapeutically.

Distribution: Red blood cells (RBCs) appear to be the storage depot for folate, as RBC levels remain elevated for periods in excess of 40 days following discontinuation of supplementation. Plasma protein binding studies showed that L-methylfolate is 56% bound to plasma proteins. Pyridoxal is stored mainly in the liver, with small amounts in the brain and muscles. The total body storage for adults is between 16 to 27mg. Pyridoxal and pyridoxal phosphate are the primary forms of Vitamin B6 in the blood. Pyridoxal phosphate is 100% protein-bound. Conversion of pyridoxine to pyridoxal phosphate and pyridoxamine to pyridoxamine phosphate takes place in erythrocytes. Pyridoxal crosses the placenta, with fetal concentrations five times that of maternal plasma concentrations. Pyridoxal is oxidized in the liver to produce 4-pyridoxic acid.

QA 84-22

Rev 09-22/01NQ

Methylcobalamin is extensively bound to specific plasma proteins called transcobalamins; transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. Vitamin B12 is stored in the liver. Methylcobalamin diffuses across the placenta and also appears in breast milk. **Excretion:** L-methylfolate is a water soluble molecule which is primarily excreted via the kidneys. Pyridoxal and Pyridoxamine are excreted in urine in small amounts 0.5 to 0.7mg daily. Major urinary metabolite: inactive form 4-pyridoxic acid. Methylcobalamin is excreted in the bile, and undergoes extensive enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours; urinary excretion, however, accounts for only a small fraction in the reduction of total body stores acquired by dietary means. 40-80% of the cumulative amount of total methyl cobalamin excreted in the urine by 24 hours after single-dose administration was excreted within the first 8 hours. **Elimination Half-life:** L-methylfolate is a water soluble molecule which is primarily excreted via the kidneys. The mean elimination half-life is approximately 3 hours for L-methylfolate after the administration of 5mg of oral L-methylfolate.

Methylcobalamin: 12.5 hours (single-dose oral administration; calculated from the average of 24-48 hour values).

CONTRA-INDICATIONS: If hypersensitive to any of its ingredient.

PRECAUTIONS:

General: Folic acid, when administered as a single agent in doses above 0.1mg daily, may obscure the detection of B12 deficiency (specifically, the administration of folic acid may reverse the hematological manifestations of B12 deficiency, including pernicious anemia, while not addressing the neurological manifestations). L-methylfolate may be less likely than folic acid to mask vitamin B12 deficiency. Folate therapy alone is inadequate for the treatment of a B12 deficiency.

Pregnancy: Category "C": Use with caution if benefits outweigh risks.

Lactation: it is not known if it is excreted in breast milk, use with caution.

DRUG INTERACTIONS: Pyfomin added to other Drugs: High dose folic acid may result in decreased serum levels for pyrimethamine and first generation anticonvulsants (carbamazepine, fosphenytoin, phenytoin, phenobarbital, primidone, valproic acid, valproate). This may possibly reduce first generation anticonvulsants effectiveness and/or increase the frequency of seizures in susceptible patients. While the concurrent use of folic acid and first generation anticonvulsants or pyrimethamine may result in decreased efficacy of anticonvulsants, no such decreased effectiveness has been reported with the use of L-methylfolate. Nevertheless, caution should be used when prescribing Pyfomin among patients who are receiving treatment with first generation anticonvulsants or pyrimethamine. Pyridoxal 5'-phosphate should not be given to patients receiving the drug levodopa, because the action of levodopa is antagonized by pyridoxal 5'-phosphate. However, pyridoxal 5'-phosphate may be used concurrently in patients receiving a preparation containing both carbidopa and levodopa.

Drugs added to Pyfomin: Antibiotics may alter the intestinal microflora and may decrease the absorption of methylcobalamin. Cholestyramine, colchicine or colestipol may decrease the enterohepatic re-absorption of methylcobalamin. Metformin, para-aminosalicylic acid and potassium chloride may decrease the absorption of methylcobalamin. Nitrous oxide can produce a functional methylcobalamin deficiency. Methotrexate, alcohol (in excess), sulfasalazine, cholestyramine, colchicine, colestipol, L-dopa, methylprednisone, NSAIDs (high dose), pancreatic enzymes (pancrelipase, pancratin), pentamidine, pyrimethamine, smoking, triamterene, and trimethoprim may decrease folate plasma levels. Warfarin can produce significant impairment in folate status after a 6-month therapy.

ADVERSE REACTIONS: While allergic sensitization has been reported following both oral and parenteral administration of folic acid, allergic sensitization has not been reported with the use of Pyfomin. Acne, skin reactions, allergic reactions, photosensitivity, nausea, vomiting, abdominal pain, loss of appetite, increased liver function test results, paresthesia, somnolence, nausea and headaches have been reported with pyridoxal 5'-phosphate. Mild transient diarrhea, polycythemia Vera, itching, transitory exanthema and the feeling of swelling of the entire body has been associated with methyl cobalamin.

INSTRUCTIONS: Store below 30° C. Protect from heat, light and moisture. Keep out of the reach of children.

PRESENTATION: Pyfomin tablets are available in a pack of 20 tablets with 2 blister of 10 tablets.

خوراک: دو ٹیبلٹ کی ہدایت کے مطابق استعمال کریں۔

ہدایت: 30° C ذریعہ سے کم درجہ حرارت پر رکھیں۔ گرمی، روشنی اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔



Manufactured for:
Nabiqasim Industries (Pvt.) Ltd.
17/24, Korangi Industrial Area,
Karachi-Pakistan.

Product E. No. C-110141

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