



NATURE'S ACTIVE FOLATE FOR PRENATAL CARE

Névo® Caplets

Névo® is a medical food for use only under medical supervision for the dietary management of impaired metabolic processes in women under a doctor's care who face high to intermediate risk pregnancies and are unable to fully metabolize or absorb folic acid.

Description

Each oval coated pink colored caplet contains:

Dietary Ingredients:

| | |
|---|----------|
| L-methylfolate Calcium (as Metafolin®)* | 1.13mg** |
| Iron (as polysaccharide iron complex) | 29mg |
| Vitamin C (ascorbic acid) | 80mg |
| Vitamin D3 (cholecalciferol) | 400IU |
| Vitamin E (dl-alpha-tocopheryl acetate) | 30 IU |
| Vitamin B1 (thiamine as thiamine mononitrate) | 3mg |
| Vitamin B2 (riboflavin) | 3.4mg |
| Vitamin B3 (niacinamide) | 20mg |
| Vitamin B5 (pantothenic acid as d-calcium pantothenate) | 7mg |
| Vitamin B6 (pyridoxine as Pyridoxine HCl) | 2.6mg |
| Vitamin B9 (folic acid) | 0.4mg |
| Vitamin B12 (cyanocobalamin) | 0.5mg |
| Biotin | 0.03mg |
| Copper (as copper oxide) | 2.0mg |
| Zinc (as zinc oxide) | 15mg |
| Calcium (as calcium carbonate) | 200mg |
| Magnesium (as magnesium oxide) | 40mg |

*CAS# 151533-22-1 is the registry of the absolute stereochemistry of L-methylfolate calcium.

**1.13mg L-Methylfolate Calcium is the molar equivalent of 1.0mg folic acid

Ingredients

Calcium (as calcium carbonate), Vitamin C (as ascorbic acid), Corn Starch, Magnesium (as magnesium oxide), Iron (as polysaccharide iron complex), Mono & Diglycerides, Microcrystalline Cellulose, Vitamin E (dl-alpha-tocopheryl), Gelatin, Hypromellose, Acacia, Crospovidone, Vitamin B3 (niacinamide), Zinc (as zinc oxide), Titanium Dioxide, Polydextrose, Vitamin B5 (pantothenic acid as d-calcium pantothenate), Dicalcium Phosphate, Magnesium Stearate, Sucrose, Polyethylene Glycol, Sodium Citrate, Silicon Dioxide, Vitamin B2 (riboflavin), Vitamin B6 (pyridoxine as pyridoxine HCl), Vitamin B1 (thiamine as thiamine mononitrate), Citric Acid, Partially Hydrogenated Vegetable Oil, Copper (as copper oxide), Triacetin, Sorbic Acid, L-methylfolate Calcium (as Metafolin®), Sodium Benzoate, Triglycerides, Vitamin B12 (cyanocobalamin), Vitamin B9 (folic acid), FD&C Red #40 Lake, FD&C Yellow #6 Lake, Carnauba Wax, Biotin, Butylated Hydroxytoluene, Sodium Alumino-Silicate, Vitamin D3 (cholecalciferol), Sodium Lauryl Sulfate.

***Metafolin® (L-methylfolate calcium) is a substantially diastereoisomerically pure source of L-methylfolate containing not more than 1% D-methylfolate which results in not more than 0.011 milligrams of D-methylfolate in Névo®.**

Névo® caplets do not contain lactose, yeast or gluten.

Indication and Usage

Névo® caplets are for the specific dietary management of impaired metabolic processes in those women with distinct nutritional requirements for any of the following conditions: hyperhomocysteinemia during pregnancy^{4,5,6,7}; high risk recurrent pregnancy loss^{5,7}; impaired folic acid absorption^{2,3}; impaired metabolism due to 677C-T mutations in the methylenetetrahydrofolate reductase gene^{8,10,11}; and dysfunctional folic acid metabolism^{11,12}. Névo® should only be used under medical supervision.

Rationale for Distinct Nutritional Requirements

Medical foods are intended for a patient who has a limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients, or who has other special medically determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone.

Névo® contains folate in the form of L-methylfolate which is the biologically active folate isomer. L-methylfolate is the body's preferred form of folate because it is directly usable by the human organism for certain metabolic processes. There are well documented studies^{2,3,6,8,12} which have established folic acid's ineffectiveness regarding inherited disorders of folate transport and metabolism. These disorders limit and impair the capacity to ingest, digest, absorb or metabolize folic acid. Folic acid, the synthetic form of folate, must be metabolized in a four step process by the body to become the

biologically active L-methylfolate. Unmetabolized levels of folic acid were found in 78% of plasma samples from women given >400 mcg of folic acid per day¹. Unmetabolized folic acid has a high affinity to bind to the cellular folate transport mechanism. This has been shown to reduce the transfer of the active metabolite L-methylfolate across the blood brain barrier^{2,3}.

D-methylfolate or 6(R)-5-methyltetrahydrofolate [6(R)-5-MTHF] is the other diastereoisomer of folate. Studies administering doses of 2.5 mg per day or higher resulted in plasma protein binding of D-methylfolate higher than L-methylfolate causing a significantly higher renal clearance of L-methylfolate when compared to D-methylfolate.⁴ Further, D-methylfolate is found to be stored in tissues in the body, mainly in the liver. D-methylfolate is not metabolized by the body and has been hypothesized to inhibit regulatory enzymes related to folate and homocysteine metabolism and reduces the bioavailability of L-methylfolate.⁵

Hyperhomocysteinemia is an independent risk factor of vascular and endothelial dysfunction in maternal patients. Although hyperhomocysteinemia is not due to folate deficiencies alone, it can be indicative of dietary deficiencies of essential nutrients, increased catabolism, clearance and excretion of essential nutrients, hormonal influence on folate metabolism or an intrinsic metabolic disorder. Increased homocysteine levels can also increase the risk of recurrent early pregnancy loss as well as increase maternal complications. Disturbed homocysteine metabolism has also been shown to have a greater effect in women with early pregnancy losses^{4,5,6,7}. In the cell, 6(S)-5-MTHF (L-methylfolate) is used in the methylation of homocysteine.

The prevalence of the 677C-T mutations in the methylenetetrahydrofolate reductase gene in pregnant women was shown to be 53%⁸. Studies show that enzyme activity necessary to convert folic acid to its active form (L-methylfolate) can be reduced by as much as a 72% in patients with the 677C-T mutation in the methylenetetrahydrofolate reductase gene⁹. In certain studies, women with the 677C-T mutation in the methylenetetrahydrofolate reductase gene (MTHFR) had significantly higher risk for recurrent pregnancy loss, congenital abnormalities and other adverse pregnancy outcomes^{10,11}. Other MTHFR gene variants (A1298C and MTHFD) that affect folic acid bioavailability have been associated with folate metabolism and the incidence of congenital anomalies^{11,12}.

Contraindications

Known hypersensitivity to any of the components in this product is a contraindication.

WARNING: Accidental overdose of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately.

Precautions

Folates, when administered as a single agent in doses above 0.1 mg daily, may obscure pernicious anemia in that hematologic remission can occur while neurological manifestations remain progressive.

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 Metafolin®. Paresthesia, somnolence, nausea and headaches have been reported with pyridoxine hydrochloride. Mild transient diarrhea, polycythemia vera, itching, transitory exanthema and the feeling of swelling of the entire body have been associated with cyanocobalamin.

Drug Interactions

Pyridoxine hydrochloride should not be given to patients receiving the drug levodopa, because the action of levodopa is antagonized by pyridoxine hydrochloride. However, pyridoxine hydrochloride may be used concurrently in patients receiving a preparation containing both carbidopa and levodopa. While the concurrent use of phenytoin and folic acid may result in decreased phenytoin effectiveness, no such decreased effectiveness has been reported with the use of Metafolin®. Capecitabine (Xeloda®) toxicity may increase with the addition of leucovorin (5-formyltetrahydrofolate) (folate).

Patient Information

Névo® should only be used under medical supervision.

Dosage and Administration

Usual adult dose is one caplet daily or as directed by your medical practitioner.

How Supplied

Available as an oval coated pink colored caplet. Névo® caplet is debossed with a "fleur-de-lis" symbol on one side and an "N" on the other side. Commercial product is supplied in bottles of 90 caplets or 500 caplets. Sample product is supplied in a carton containing five blisters with one caplet in each blister or a bottle of 4 caplets.

Commercial Product (90 caplets) 0525-2010-90*
Commercial Product (500 caplets) 0525-2010-50*
Sample Product (5 blisters) 0525-2010-05*
Professional Samples – Not for sale
Sample Product (bottle 4 caplets) 0525-2010-04*
Professional Samples – Not for sale

*Pamlab, LLC does not represent this product code to be a National Drug Code (NDC) number. Instead, Pamlab has assigned a product code formatted according to standard industry practice to meet the formatting requirements of pharmacy and health insurance computer systems.

Storage

Store at controlled room temperature 15°C to 30°C (59°F to 86°F) (See USP). Protect from light and moisture.

KEEP THIS OUT OF THE REACH OF CHILDREN.

Patents

Some or all of the following patents may apply:
U.S. Patent No. 5,563,126 U.S. Patent No. 5,795,873
U.S. Patent No. 5,997,915 U.S. Patent No. 6,011,040
U.S. Patent No. 6,254,904 U.S. Patent No. 6,254,904
U.S. Patent No. 6,297,224 U.S. Patent No. 6,528,496
and other pending patent applications.

References

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PAMLAB, L.L.C. Covington, LA 70433
PC-0053 Revised 2/10

