

Nufola®

NDC 58407-3512-60

Dietary Supplement

DESCRIPTION Nufola is an orally administered dietary supplement for patients that want to support a healthy nervous system through dietary supplementation.

INGREDIENTS

Serving Size: 1 - 2 Capsules
Servings Per Container: 30
Each capsule contains: Vitamin B-6 (Pyridoxal 5-Phosphate) 25 mg, Folate [as 3,500 (3.5 mg) mcg DFE (dietary folate equivalent) L-5-methyltetrahydrofolic acid calcium salt], Vitamin B-12 (Methylcobalamin) 1 mg, Alpha Lipoic Acid 300 mg
Other Ingredients: Hard Vegetable Capsule (Hypromellose, Purple Carrot), Water, Long Grain White Rice Flour, Magnesium Stearate (Vegetable Grade), Silicon Dioxide (Siernat *50 S)

ADMINISTRATION Nufola is to be administered orally, one or two daily. Capsules are intended to be swallowed whole with water. Use of Nufola should always occur under medical supervision.

PHARMACOLOGY

5-MTHF Calcium Salt is a new dietary ingredient (NDI) that shows enhanced stability and bioavailability when compared to folic acid. 5-methyltetrahydrofolic acid salt (5-MTHF) is the primary biologically active isomer of folate. Unlike supplementary folic acid, which requires enzymatic reduction by the methylenetetrahydrofolate reductase enzyme (MTHFR) to become biologically active, L-methylfolate calcium salt is able to penetrate cellular membranes without requiring metabolism.

Therapeutically, L-methylfolate calcium salt is used to reduce homocysteine levels and to improve vascular endothelial function through its influence on nitric oxide (NO). Clinical studies have shown that direct supplementation with L-methylfolate calcium salt reduces homocysteine levels and increases plasma folate levels more effectively than folic acid.

In fact, folic acid supplementation alone was shown not to reduce intracellular homocysteine. Inborn genetic variations (polymorphisms) in the MTHFR gene are the most common genetic causes for elevated homocysteine levels.

Pyridoxal 5-phosphate (P5P) is the metabolically active coenzyme form of vitamin B6. P5P-dependent enzymes are involved in many biochemical reactions, including the transsulfuration of homocysteine and decarboxylation of amino acids that yield biogenic amines (neurotransmitters).

Methylcobalamin is a vitamin B12 analog that is neurologically active and is necessary for nervous system function. Methylcobalamin's neuroprotective effects may be mediated by the methylation cycle. In conjunction with supplemented folate, the addition of Vitamin B12 has been shown to reduce homocysteine more than folic acid alone. Clinical trials suggest the combination of 5-MTHF, P5P and methylcobalamin can support a healthy nervous system.

Alpha-lipoic acid (ALA) is a multifunctional antioxidant that is orally absorbed and converted to its reduced form (dihydrolipoic acid or DHLA) in many tissues. The redox couple effects of ALA/DHLA are important in biological processes, including the regulation of gene expression and the modulation of enzyme and receptor activities; these mechanisms have important implications relating to various metabolic processes.

METABOLIC AND VASCULAR/HYPOXIC FACTORS IN PERIPHERAL NEUROPATHY (PN)

Research suggests that the underlying pathology of PN involves a complex interaction between metabolic and vascular factors that converges on nerves and the endothelium of the peripheral microvasculature. Elevated levels of homocysteine (hyperhomocysteinemia, HHcy) is considered an independent risk factor for the development of PN. HHcy inhibits endothelium-mediated nitric-oxide-dependent vasodilation and is thought to contribute to endothelial dysfunction (ED). ED is complex, involving multiple mechanisms, not the least of which are HHcy, oxidative stress, and the resulting reduced bioavailability of nitric oxide (NO). With respect to peripheral nerves, insufficient NO causes vasoconstriction and therefore reduced blood flow to peripheral nerves. Reduced blood flow translates into the inadequate transfer of nutrients to peripheral nerve cells and consequent nerve damage. Alternately, studies suggest that enhancing endothelial function and reversing some of these factors that interfere with NO production will increase NO, improve blood flow through

vasodilation, enable the delivery of essential nutrients and oxygen to peripheral nerves, and thereby allow the nerves to perform normal functions. Nufola is designed to address metabolic and vascular processes, and support a healthy nervous system.

INDICATIONS AND USAGE Nufola capsules are indicated for the specific dietary requirements of patients to support a healthy nervous system. Nufola should always be used under medical supervision.

CONTRAINDICATIONS Nufola is contraindicated in children, pregnant or nursing women, women of childbearing age who may become pregnant, and anyone with a known hypersensitivity to any of the components. ALA is contraindicated in individuals who are thiamine deficient.

PRECAUTIONS Patients taking agents that lower blood pressure, affect blood sugar levels, or increase bleeding risk should be monitored. High-dose folic acid intake without concurrent B12 supplementation may mask the symptoms of pernicious, aplastic, or normocytic anemias caused by vitamin B12 deficiency. 5-MTHF is unlikely to mask B12 deficiency.

ADVERSE REACTIONS Patients taking a combination of B vitamins at levels that are comparable to those found in Nufola have reported numbness in two fingers, dizziness, and balance disorder. Folic acid supplementation has been reported to cause gastrointestinal (GI) distress, irritability, excitability, sleep disturbances, and allergic reactions in some individuals. Human trials using 0.4 to 17 mg/day of 5-MTHF showed an absence of adverse effects. Paresthesia, somnolence, nausea, and headaches have been reported with pyridoxal 5-phosphate [coenzyme form of Vitamin B6]. Doses of B6 under 200 mg/d are not likely to cause adverse effects unless an individual is particularly sensitive. Neurological and GI disturbances and skin reactions have been reported. Excessive doses may cause reversible sensory neuropathy. Vitamin B12 may cause GI disturbances, polycythemia vera, or allergic reactions in sensitive individuals. ALA may cause mild skin rash, GI complaints, or dizziness; these are primarily associated with doses over 1200 mg/d. This is not a comprehensive list of adverse reactions, others may occur. Consult a current, comprehensive database for all potential adverse reactions.

DRUG INTERACTIONS Folic acid could decrease the effectiveness of methotrexate, pyrimethamine, and anti-seizure medications/first-generation anticonvulsants (phenytoin, carbamazepine, valproate, fosphenytoin, phenobarbital, primidone, for example). It is not known if 5-MTHF has the same interactions, so caution is recommended when prescribing Nufola among patients who are taking these medications. Vitamin B6 may exacerbate photosensitivity caused by amiodarone. Pyridoxal 5-phosphate (B6) may also affect metabolism and may therefore decrease the effectiveness of levodopa, phenobarbital, and phenytoin. Pyridoxal 5-phosphate (B6) should not be given to patients receiving the drug levodopa, because the action of levodopa is antagonized by Pyridoxal 5-phosphate (B6). However, Pyridoxal 5-phosphate (B6) may be used concurrently in patients receiving a preparation containing both carbidopa and levodopa. Vitamin B12 should not be combined with chloramphenicol. Alpha-lipoic acid may interact with thyroid medications. Theoretically, concomitant use of alpha-lipoic acid with anti-diabetic drugs may have an additive effect. This is not a complete list of drug interactions. Talk to your doctor or pharmacist before using any other prescription or over-the-counter medicines or herbal/health supplements with Nufola.

STORAGE: Store at 20° to 25° C (68° to 77° F), the controlled room temperature defined by the U.S. Pharmacopeia (USP).

HOW SUPPLIED: Nufola vegetable capsules are supplied in a bottle of 60 count 58407-3512-60 and in a sample size package of four per box, 58407-3512-04.

REFERENCES: 1. Stahl, S. M. CNS Spectrums 2007; 12(10):739-744. 2. Kelly CB, McDonnell AP, Johnston TG et al. J Psychopharmacol, 2004; 18(4):567-571. 3. Evans, J.L. and Goldfine, I.D. (2000) Diabetes Technol Therap 2: 401-413 4. Evans, J.L. et al (2003) Diabetes: From Research to Diagnosis and Treatment, Chapter 29: 479-496. 5. Diabetes Care 29:2365-2370, 2006.

KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

Sensations of tingling, burning & numbness in your arms, hands, legs & feet may be the result of damaged nerves and blood vessels.

Take a NU Step in Life!



Nufola®

An important dietary supplement containing absorbable forms of folate, B-12, B-6, and ALA

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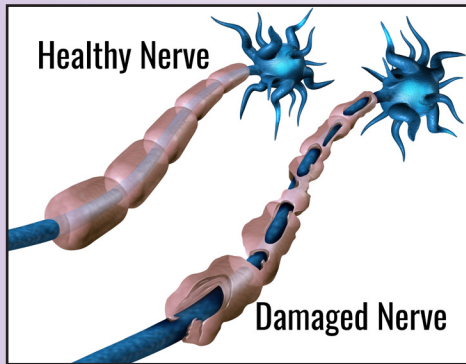
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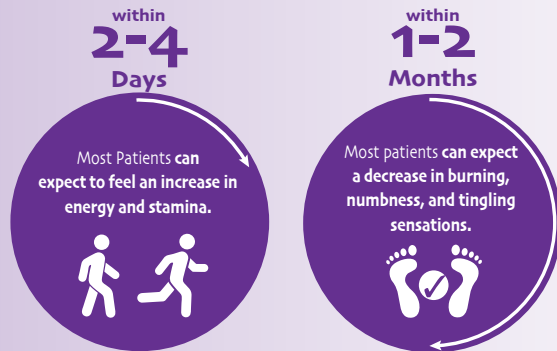
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Some Patients who exhibit symptoms of neuropathy have an unmet dietary need...

Nerve and blood vessel damage can reduce quality of life.^{3,4 & 5} Damage is caused by free radicals, inflammation, and high homocysteine levels, which may result from inadequate folate and/or B vitamin absorption. Symptoms include fatigue, weakness, tingling in arms or legs, dizziness, mood changes, and mouth sores.



Age, weight, medications, nutrition, and genetics are among the factors that affect one's ability to absorb & produce sufficient folate.¹ 70% of people in the United States lack a necessary enzyme (MTHFR) to metabolize folic acid into folate; folate is an essential vitamin for nerve & blood vessel repair & function.²



Take a *NU* Step in Life!

Improved Folate, B-12, B-6, & ALA Absorption.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

Take a *NU* Step in Life!

Nufola® is not your average dietary supplement...

How is Nufola different?

First, Nufola is a dietary supplement, which is specifically designed to help manage problems associated with damaged nerves and blood vessels.

Second, Nufola contains absorbable B vitamins which help repair nerves and muscles (and provide energy and vigor), unlike many of the B vitamins used in store bought vitamins. What good is a vitamin that is not absorbed by our bodies?

Third, Nufola contains ALA (alpha lipoic acid). ALA reduces the free radical damage and inflammation that are associated with blood vessel complications, including with diabetes.^{3, 4 & 5}

Fourth, Nufola contains the absorbable folate form, L-methylfolate calcium salt. Nufola contains readily absorbable folate that is not folic acid! So, the body does not need the MTHFR enzyme (which many people lack) to absorb the folate in Nufola!

Each Nufola capsule contains (in bioactive forms):

Vitamin B6 (as pyridoxal 5-phosphate) 25mg

L-methylfolate (L-5-MTHF calcium salt) 3.5mg (3,500 mcg DFE)

Vitamin B12 (as methylcobalamin) 1mg

Alpha-Lipoic Acid 300mg

Nufola is not expensive (approximately \$1/day).

Check with your pharmacy or order directly from us online at www.magnaweb.com

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