

# NeuroDHA®

NATURE'S ACTIVE FOLATE FOR PRENATAL CARE

NeuroDHA® 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

NeuroDHA® is an opaque blue gelatin capsule.

## Description of Primary Ingredients:

Algidha™ proprietary blend.....	6887mg*
Calcium (tricalcium phosphate).....	200mg
Vitamin C (ascorbic acid).....	40mg
Elemental iron (ferrous fumarate).....	27mg
Vitamin B6 (pyridoxine HCl).....	25mg
Vitamin E (d-alpha-tocopherol).....	30IU
L-methylfolate Calcium (as Metafolin®).....	*1.13mg**
Vitamin B12 (methylcobalamin).....	1mg
Vitamin B9 (folic acid).....	400 mcg

\*Algidha™ is a proprietary blend containing algal oil and soy lecithin.

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

\*\*\*1.13mg L-Methylfolate (calculated as L-methyltetrahydrofolic acid) is the molar equivalent of 1.06mg folic acid.

\*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 NeuroDHA®.

## Indication and Usage

NeuroDHA® capsules 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<sup>1,5,6,7</sup>; high risk recurrent pregnancy loss<sup>8,9</sup>; risk of anemia due to impaired folic acid absorption<sup>5,6,10,11,12</sup>; and impaired metabolism due to 677C-T mutations in the methylenetetrahydrofolate reductase gene<sup>10,11</sup>. NeuroDHA® 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 medical determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone.

NeuroDHA® 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<sup>13-16,17</sup> 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 day<sup>1</sup>. 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<sup>2,3</sup>.

D-methylfolate or (6R)-5-methyltetrahydrofolate ((6R)-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.<sup>18</sup> 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.<sup>2</sup>

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 carbamoyl, 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 increased maternal complications. Disturbed homocysteine metabolism has also been shown to have a greater effect in women with early pregnancy losses<sup>4,6,7</sup>. In the cell, (6S)-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%. Studies show that enzyme activity necessary to convert folic acid to its active form (L-methylfolate) can be reduced by as much as 72% in patients with the 677C-T mutation in the methylenetetrahydrofolate reductase gene. 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 T1012C) that affect folic acid bioavailability have been associated with folate metabolism and the incidence of congenital anomalies<sup>11,12</sup>.

## Contraindications

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

## Warnings

Ingestion of more than 3 grams per day of omega-3 fatty acids has been shown to have potential antithrombotic effects, including bleeding time and INR. Administration of omega-3 fatty acids should be avoided in patients on anticoagulants and in those known to have an inherited or acquired bleeding diathesis.

**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 0.1mg 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®.

## 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®. Caprecaibine (Xeloda®) toxicity may increase with the addition of leucovorin (5-formyltetrahydrofolate) (folate).

## Patient Information

NeuroDHA® should only be used under medical supervision.

NeuroDHA® is certified kosher by Triangle K and Associates.

## Contains Soy



## Dosage and Administration

Usual adult dose is 1 (one) gelatin capsule daily or as directed by your physician.

## How Supplied

Available as a blue, soft gelatin capsule with "Neuro DHA" imprinted on one side in white ink. Commercial product (0525-0621-30) is supplied in bottles of 30 capsules. Sample product (0525-0621-04) is supplied in bottles of 4 capsules.

Commercial Product (30 capsules) 0525-0621-30\* Use under medical/physician supervision.

Sample Product (4 capsules) 0525-0621-04\* 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. Dispense commercial product in original container. Dispense sample product in original container.

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

## Patents

Some or all of the following patents may apply:

U.S. Patent No. 6,207,651	U.S. Patent No. 6,011,040
U.S. Patent No. 5,563,126	U.S. Patent No. 6,254,904
U.S. Patent No. 5,795,873	U.S. Patent No. 6,297,224
U.S. Patent No. 5,997,915	U.S. Patent No. 6,528,496

and other pending patent applications.

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