

CEREFOLIN®

A medical food for the dietary management of hyperhomocysteinemia.

Description

Each round coated blue colored tablet contains:

Dietary Ingredients:

L-Methylfolate (Metafolin®)	5.635 mg
Riboflavin (B ₂)	5 mg
Pyridoxine (B ₆)	50 mg
Cyanocobalamin (B ₁₂)	1 mg

Other Ingredients:

Microcrystalline Cellulose, Opadry II Blue #40L10890, Stearic Acid Vegetable Source, Croscarmellose Sodium, Silicon Dioxide, Magnesium Stearate Vegetable Source and Opadry II Clear #Y-19-7483.

CEREFOLIN® tablets do not contain sugar, lactose, yeast or gluten.

Indication and Usage

CEREFOLIN® tablets are indicated for the distinct nutritional requirements of individuals under a physician's treatment for hyperhomocysteinemia; with particular emphasis for individuals diagnosed with or at risk for mild to moderate: cognitive impairment¹, vascular dementia², or Alzheimer's disease³.

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. The 1 mg of cyanocobalamin contained in **CEREFOLIN®** has been shown to provide an adequate amount of cyanocobalamin to address this precaution⁴. A safe upper limit of 100 mg per day has been established for the unsupervised medical use of pyridoxine. Consider all sources of pyridoxine supplementation when prescribing **CEREFOLIN®**.

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. Mild transient diarrhea, polycythemia vera, itching, transitory exanthema and the feeling of swelling of the entire body has been associated with cyanocobalamin. Transient headaches have been reported infrequently with the use of **CEREFOLIN®**. If headaches should occur with the use of **CEREFOLIN®** consult with your physician.

Contraindications

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

Drug Interactions

Pyridoxine should not be given to patients receiving the drug levodopa, because the action of levodopa is antagonized by pyridoxine. However, pyridoxine 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®.

Patient Information

CEREFOLIN® is a medical food for use only under the direction and supervision of a licensed physician.

Dosage and Administration

Usual adult dose is one to two tablets daily or as directed by a physician.

CEREFOLIN® is not recommended for use with children under the age of twelve.

How Supplied

Available as a round coated blue colored tablet. Debossed with "PAL" on one side and "M5" on the other. Commercial product is supplied in bottles of 90 or 500 tablets. Sample product is supplied in a tri-fold carton containing two tablets.

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 (90 tablets) in original light-resistant container. Dispense sample product in original blister.

Commercial Product (90 tablets)
0525-0503-90 Rx Only

Cerefolin

Commercial Product (500 tablets)
0525-0503-50 Rx Only
Sample Product (2 tablets)
0525-0503-02 Professional
Samples – Not for sale.

Patents

Some or all of the following patents may apply:
U.S. Patent No. 4,940,658
U.S. Patent No. 6,207,651
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
U.S. Patent No. 6,011,040
and other pending patent applications.

References

¹ Lehmann M, Regland B, Blennow K, and Gottfries CG: Vitamin B₁₂-B₆-Folate Treatment Improves Blood-Brain Barrier Function in Patients with Hyperhomocysteinemia and Mild Cognitive Impairment. *Dementia and Geriatric Cognitive Disorders* 2003;16:145-150.

² Nilsson K, Gustafson L, and Hultberg B: Improvement of cognitive functions after cobalamin/folate supplementation in elderly patients with dementia and elevated plasma homocysteine. *International Journal of Geriatric Psychiatry* 2001;16:609-614.

³ Seshadri S, Beiser A, Selhub J, Jacques PF, Rosenberg IH, D'Agostino RB, Wilson PWF, and Wolf PA: Plasma Homocysteine As A Risk Factor For Dementia And Alzheimer's Disease. *New England Journal of Medicine* 2002;Vol346, No. 7:476-483.

⁴ Lederle FA: Oral cobalamin for pernicious anaemia: medicine's best kept secret? *JAMA* 1991;265:94-95.

Metafolin® is a trade mark of Merck KGaA, Germany.

Manufactured For

PAMLAB, L.L.C.
Covington, LA 70433 1/05

MERCK EXHIBIT 2265
Gnosis v Merck & Cie
IPR2013-00117

MERCK ITC 02 00105735