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CLINICAL ALERT[®]

Dear Healthcare Professional,

At *MPR*, we strive to bring you important drug information in a concise and timely fashion. In keeping with this goal, we are pleased to bring you this **CLINICAL ALERT** for **CerefolinNAC[®]** (L-methylfolate [**Metafolin[®]**], methylcobalamin, N-acetylcysteine) Caplets, from PAMLAB, L.L.C.

CerefolinNAC, a prescription medical food, is indicated for the dietary management of patients identified with or under a physician's treatment for early memory loss.¹ Patients diagnosed with or those at risk for neurovascular oxidative stress and/or hyperhomocysteinemia, as well as mild to moderate cognitive impairment (with or without vitamin B₁₂ deficiency), vascular dementia, and Alzheimer's disease are candidates for treatment with CerefolinNAC.¹

CerefolinNAC is taken once daily and does not require titration to reach a target dose or tapering to avoid withdrawal.¹ The ingredients in CerefolinNAC have a low potential for drug interactions.¹ CerefolinNAC does not interfere with anticholinergic drugs or second generation anticonvulsants; high doses of folate, as in CerefolinNAC, may reduce the effectiveness of first-generation anticonvulsants.¹

CerefolinNAC does not contain sugar, lactose, yeast, or gluten.¹

More information about CerefolinNAC is available in the current edition of *MPR*.

For your reference, please see the enclosed full [Prescribing Information](#) for CerefolinNAC.

Sincerely,

Grace L. McBride
Editorial Director
MPR Custom Programs

REFERENCE

1. CerefolinNAC[®] [package insert]. Covington, LA; PAMLAB, LLC; 2009.

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CLINICAL ALERT

CEREFOLINNAC[®]

(L-methylfolate [Metafolin[®]], methylcobalamin, N-acetylcysteine) Caplets

Company: PAMLAB, L.L.C.

Pharmacologic Class: Medical food

Active Ingredients: L-methylfolate, methylcobalamin, N-acetylcysteine; caplets; sugar-, lactose-, yeast-, and gluten-free.

Indications: Dietary management of patients identified with or under a physician's treatment for early memory loss, with emphasis on those at risk for neurovascular oxidative stress and/or hyperhomocysteinemia; mild to moderate cognitive impairment with or without vitamin B₁₂ deficiency, vascular dementia, or Alzheimer's disease.

Adult Dose: 1 caplet daily.

Children's Dose: Not recommended.

Precautions: Avoid if renal stones occur. Do not administer to critically ill patients. Folic acid may mask pernicious anemia. History of peptic ulcer. Chronic liver disease. Pre-term newborns. Nursing mothers: not recommended.

Interactions: May antagonize first generation anticonvulsants (eg, carbamazepine, fosphenytoin, phenytoin, phenobarbital, primidone, valproic acid, valproate), or pyrimethamine; caution with second generation anticonvulsants. Concomitant nitrates: increased risk of headaches. Capecitabine toxicity increased with addition of leucovorin. May produce false-positive result in nitroprusside test for ketone bodies. Absorption of methylcobalamin

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Therapy for early memory loss

may be decreased with antibiotics, metformin, para-aminosalicylic acid, potassium chloride. Cholestyramine, colchicine, colestipol may decrease re-absorption of methylcobalamin. Nitrous oxide may produce functional methylcobalamin deficiency. Folate levels may be reduced by anticonvulsants, methotrexate, alcohol (excess amounts), sulfasalazine, cholestyramine, colchicine, colestipol, isotretinoin, L-dopa, methylprednisone, NSAIDs (high dose), oral contraceptives, pancreatic enzymes, pentamidine, pyrimethamine, smoking, triamterene, trimethoprim.

Adverse Reactions: GI upset, polycythemia vera, itching, transitory exanthema, swelling, headache, rash (with or without fever); rare: renal stones.

How Supplied: Caplets—90, 500

✓ **CerefolinNAC is indicated to meet the unique nutritional requirements of individuals with early memory loss¹**

✓ **Early memory loss may occur in individuals who are diagnosed with or at risk for¹**

- Neurovascular oxidative stress and/or hyperhomocysteinemia
- Mild or moderate cognitive impairment
 - With or without vitamin B₁₂ deficiency
- Vascular dementia
- Alzheimer's dementia

✓ **CerefolinNAC is comprised of 3 active ingredients¹**

ACTIVE INGREDIENTS

L-methylfolate	5.6 mg
Methylcobalamin	2 mg
N-acetylcysteine	600 mg

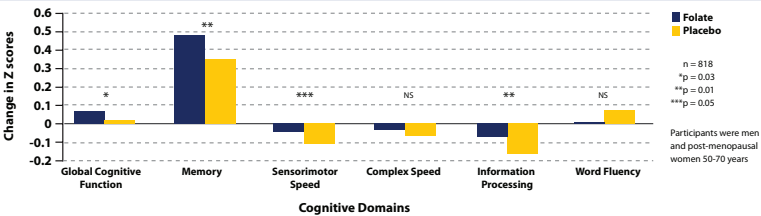
Source: CerefolinNAC [package insert].¹

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CLINICAL ALERT

- ✓ **N-acetylcysteine (NAC) is a precursor to glutathione (GSH)¹**
 - GSH, which decreases with age, helps neurovascular tissue metabolize vitamin B₁₂ and reduce oxidative stress^{1,2}
 - GSH also lowers plasma homocysteine levels and increases total antioxidant capacity, which is needed for management of cognitive impairment¹
 - Alzheimer's disease has been associated with aging, oxidative stress, and elevated homocysteine levels^{2,3}
- ✓ **Folate has been shown to support cognitive impairment needs in those with suboptimal folate levels⁴**

CHANGE IN COGNITIVE FUNCTION ATTRIBUTED TO FOLATE



Source: Durga et al.⁴

- ✓ **In clinical studies, cobalamin and folate are needed to provide the cognitive benefits in patients with mild-moderate dementia and elevated homocysteine levels⁵**
 - Patients were assessed using the Mini-mental state examination and A short cognitive performance test for assessing memory and attention
- ✓ **Managing the metabolic processes of early memory loss helps improve⁶**
 - Patient behaviors
 - Clinical outcomes
- ✓ **CerefolinNAC provides the right balance of performance and tolerability⁷**
 - 93% of patients reported improvement after taking CerefolinNAC
 - 97% of patients tolerated CerefolinNAC
- ✓ **Clinical trial results for CerefolinNAC are expected in 2010**

Please see accompanying full Prescribing Information.

REFERENCES

1. CerefolinNAC [package insert]. Covington, LA: PAMLAB, L.L.C.; 2009.
2. Boyd-Kimball D, Sultana R, Abdul HM, Butterfield DA. Gamma-glutamylcysteine ethyl ester-induced up-regulation of glutathione protects neurons against A β (1-42)-mediated oxidative stress and neurotoxicity: implications for Alzheimer's disease. *Journal of Neuroscience Research*. 2005;79(5):700-706.
3. McCaddon A, Hudson P, Davies G, et al. Homocysteine and cognitive decline in health elderly. *Dement Geriatr Cogn*. 2001;12(5):309-313.
4. Durga J, van Boxtel PJ, Schouten EG, et al. Effects of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomized, double-blind, controlled trial. *Lancet*. 2007;369(9557):208-215.
5. Nilsson K, Gustafson L, Hultberg B. Improvement of cognitive function after cobalamin/folate supplementation in elderly patients with dementia and elevated plasma homocysteine. *International Journal of Geriatric Psychiatry*. 2001;16(6):609-614.
6. Adapted from Laura OST, NIST/ORNL Dedicate New Nuclear Medicine Lab/www.nist.gov.../techbeat/tb2006_0330.htm/ Published March 30, 2006. Accessed June 30, 2009.
7. CerefolinNAC Clinical Evaluation Patient Response Survey (May 2009).

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