

Supplement Facts

DESCRIPTION

Denovo™ is a dietary supplement used for the metabolic management of low L-methylfolate (5-MTHF) levels associated with mood disorders.

INGREDIENTS

Supplement Facts

Serving Size: 1 Capsule

Servings Per Container: 30 Days

Each Capsule Contains the following:

Folate [as 15 mg. L-5-MTHF (From L-5-methyltetrahydrofolate calcium salt)]

Other ingredients: microcrystalline cellulose, gelatin, vegetable magnesium stearate, silica, titanium dioxide, FD&C yellow #5k, FD&C yellow #6.

CLINICAL PHARMACOLOGY

Denovo™ contains L-methylfolate calcium salt which consists of a proprietary biologically-active folate. It works to assist the body with regulating the synthesis or production of neurotransmitters found in the brain, such as serotonin, norepinephrine, and dopamine. Low levels of these neurotransmitters, which may be due to a genetic abnormality that reduces the body's ability to convert folate into the active compound, 5-MTHF, have been associated with depression. It is estimated that this genetic abnormality is found in approximately 70 percent of people suffering from depression. The most common of which is called Methylene tetrahydrofolate Reductase (MTHFR) genetic polymorphism, which compromises a person's ability to convert folic acid and dietary folate into 5-MTHF.

INDICATIONS AND USE

ADJUNCTIVE USE IN MOOD DISORDERS

Denovo® is indicated for the distinct nutritional requirements of individuals who have suboptimal levels of L-methylfolate in the cerebrospinal fluid, plasma, and/or red blood cells and have major depressive disorder (MDD), with particular emphasis as adjunctive support for individuals who are on an antidepressant. **Denovo™** is indicated regardless of MTHFR C677T polymorphism genotype.⁷

CONTRAINDICATIONS: **Denovo™** is contraindicated in patients with known hypersensitivity to any of the components contained in this product.

PRECAUTIONS

Folic acid, when administered in daily doses above 0.1 mg, may obscure the detection of B12 deficiency (specifically, the administration of folic acid may reverse the hematological manifestations of B12 deficiency, including pernicious anemia, while not addressing the neurological manifestations). 5-MTHF may be less likely than folic acid to mask vitamin B12 deficiency.^{8,9} Folate therapy alone is inadequate for the treatment of a B12 deficiency.

A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed, although not established in controlled trials, that treating such an episode with an antidepressant alone may increase the likelihood of a precipitation of a mixed/manic episode in patients at risk for bipolar disorder. **Denovo™** is not an antidepressant. However, 5-MTHF has been shown to enhance antidepressant effects of known antidepressants.³ Caution is recommended in patients with a history of bipolar illness. Patients with depressive symptoms should be adequately screened to determine if they are at risk for bipolar disorder since mood elevation in this population is possible.

Denovo™ should always be used under medical supervision.

PATIENT INFORMATION: **Denovo™** is a Dietary Supplement.

INTERACTION WITH DRUGS

Before using this product, tell your doctor or pharmacist of all the products you use. Keep a list of all of your medications with you, and share the list with your doctor and pharmacist. No decrease in effectiveness of drugs has been reported with the use of **Denovo™**.

Denovo™ contains folate, which may have interactions with the following:

- Antiepileptic drugs (AED): The AED class including, but not limited to, phenytoin, carbamazepine, primidone, valproic acid, phenobarbital, and lamotrigine have been shown to impair folate absorption and increase the metabolism of circulating folate. Additionally, concurrent use of folic acid has been associated with enhanced phenytoin metabolism, lowering the level of this AED in the blood and allowing breakthrough seizures to occur.^{10,11,13,16}
- Capecitabine: Folinic acid (5-formyltetrahydrofolate) may increase the toxicity of Capecitabine.¹²
- Dihydrofolate Reductase Inhibitors (DHFRIs): DHFRIs block the conversion of folic acid to its active forms, and lower plasma and red blood cell folate levels. DHFRIs include aminopterin, methotrexate, pyrimethamine, triamterene, and trimethoprim.¹³

- Fluoxetine: Fluoxetine exerts a noncompetitive inhibition of the 5-methyltetrahydrofolate active transport in the intestine.¹⁴
- Isotretinoin: Reduced folate levels have occurred in some patients taking isotretinoin.¹⁵
- Nonsteroidal Anti-inflammatory Drugs (NSAIDs): NSAIDs have been shown to inhibit some folate dependent enzymes in laboratory experiments. NSAID examples: ibuprofen, naproxen, indomethacin, and sulindac.¹³
- Oral Contraceptives: Serum folate levels may be depressed by oral contraceptive therapy.¹³
- Methylprednisolone: Reduced serum folate levels have been noted after treatment with methylprednisolone.¹³
- Pancreatic Enzymes: Reduced folate levels have occurred in some patients taking pancreatic extracts.¹³
- Pentamidine: Reduced folate levels have been seen with prolonged intravenous pentamidine.¹³
- Metformin treatment in patients with type 2 diabetes decreases serum folate.^{17,18}
- Warfarin can produce significant impairment in folate status after a six-month therapy.¹⁹

ADVERSE REACTIONS

Allergic reactions have not been reported following the use of oral (6S)-5-methyltetrahydrofolic acid, glucosamine salt.

DOSAGE AND ADMINISTRATION

Take one capsule daily as directed by a health care professional.

STORAGE Store at 15° -30°C (59°-86°F)

HOW SUPPLIED **Denovo** yellow opaque capsules are supplied in a bottle of 30 count, NDC 58407-1500-30, and a sample size package of 3 capsules per box, 58407-1500-03.

WARNING: Protect from heat, light and moisture. Keep out of reach of children. Do not purchase if seal is broken.

REFERENCES: 10. Tatum W IV, et al. Arch Intern Med. 2004;164(2):137-45. [PMID: 14744836] 11. Wulffelé MG, et al. J Intern Med. 2003; 254(5):455-63. [PMID: 14535967] 12. Desouza C, et al. Drugs. 2002; 62(4):605-16. [PMID: 11893229] 13. Sobczyńska-Malefora A, et al. Blood Coagul Fibrinolysis. 2009 June;20(4):297-302. [PMID: 19349858]

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.

58407-1500-30

DENOVO™
15 mg. of L-methylfolate calcium salt
For improved folate levels

Pick Numbers: ABC #10192197, Cardinal #5490362, McKesson #3567054, ANDA #328855, Smith Drug #869669, Morris Dickson #496554

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*Is it possible that my
depressed feelings are a result
of a type of folate deficiency?*



A new, low-cost, active folate

DENOVO™