

# L-methylfolate Calcium 7.5 mg tablets

Rx Only

## DESCRIPTION

L-methylfolate Calcium 7.5 mg tablets are an orally administered prescription medical food for the dietary management of patients with nutritional deficiencies or are in need of nutritional supplementation. Each round, coated, blue colored tablet contains:

### Dietary Ingredients:

L-methylfolate Calcium[6(S)-5-MTHF] (as Xolafin-B™\*).....7.5 mg

### Other Ingredients:

dicalcium phosphate, microcrystalline cellulose, stearic acid, croscarmellose sodium, magnesium stearate, silica, Opadry II Blue 85F90748, clear coating

L-methylfolate Calcium 7.5 mg tablets do not contain sugar, lactose, yeast or gluten.

## CLINICAL PHARMACOLOGY

L-methylfolate or 6(S)-5-methyltetrahydrofolate [6(S)-5-MTHF], is the primary biologically active isomer of folate and the primary form of folate in circulation. It is also the form which is transported across membranes into peripheral tissues, particularly across the blood brain barrier, in contrast to folic acid which does not. In cells, 6(S)-5-MTHF is used in the methylation of homocysteine to form methionine and tetrahydrofolate (THF). THF is the immediate acceptor of one carbon unit for the synthesis of thymidine-DNA, purines (RNA and DNA) and methionine. Folic acid, the synthetic form of folate, must undergo enzymatic reduction by methylenetetrahydrofolate reductase (MTHFR) to become biologically active. Genetic mutations of MTHFR result in a cell's inability to convert folic acid to 6(S)-5-MTHF.

### Pharmacokinetics:

**Absorption and Elimination:** L-methylfolate is a water soluble molecule which is primarily excreted via the kidneys. In a study of subjects with coronary artery disease (n=21), peak plasma levels were reached in 1-3 hours following ORAL/PARENTERAL administration. Peak concentrations of L-methylfolate were found to be more than seven times higher than folic acid (129 ng/ml vs. 14.1 ng/ml) following ORAL/PARENTERAL administration. The mean elimination half-life is approximately 3 hours after 5mg of oral L-methylfolate, administered daily for 7 days. The mean values for C<sub>max</sub>, T<sub>max</sub>, and AUC<sub>0-12</sub> were 129 ng/ml, 1.3 hr., and 383 respectively.

**Distribution:** Red blood cells (RBCs) appear to be the storage depot for folate, as RBC levels remain elevated for periods in excess of 40 days following discontinuation of supplementation. Plasma protein binding studies showed that L-methylfolate is 56% bound to plasma proteins.

## INDICATION AND USAGE

L-methylfolate Calcium 7.5 mg tablets are indicated for the supplemental requirements of patients with nutritional deficiencies or are in need of nutritional supplementation.

L-methylfolate Calcium 7.5 mg tablets should always be administered under the care of a Physician.

## CONTRAINDICATIONS

There have been rare reports of hypersensitivity (allergic-like reactions) to L-methylfolate Calcium 7.5 mg tablets. Therefore, a known hypersensitivity to any of the components in the product is a contraindication to its use for any indication.

## PRECAUTIONS

### General:

Folic acid, when administered as a single agent in doses above 0.1mg daily, may obscure the detection of B<sub>12</sub> deficiency (specifically, the administration of folic acid may reverse the hematological manifestations of B<sub>12</sub> deficiency, including pernicious anemia, while not addressing the neurological manifestations). L-methylfolate may be less likely than folic acid to mask vitamin B<sub>12</sub> deficiency. Folate therapy alone is inadequate for the treatment of a B<sub>12</sub> deficiency. Folic acid, when administered in daily doses above 800 mcg, may increase the amount of unmetabolized folic acid, which has been linked to accelerated growth of existing neoplasms in the colon. L-methylfolate may be less likely than folic acid to accelerate the growth of existing neoplasms.

### Patient Information:

L-methylfolate Calcium 7.5 mg tablets are a medical food for use only under the direction and supervision of a licensed physician.

### Interaction with drugs:

No decrease in effectiveness has been reported with the use of L-methylfolate Calcium 7.5 mg tablets, however several drugs have been shown to interact with folic acid, folate metabolism, the absorption of folate, and the degradation of folate. Monitoring of folate levels may be necessary among patients who are receiving treatment with the drugs listed below.

*The interactions below are based on folic acid drug interaction reports in scientific publications.*

Drugs which interact with folate include:

- 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.
- Capecitabine: Folinic acid (5-formyltetrahydrofolate) may increase the toxicity of Capecitabine.
- Cholestyramine: Reduces folic acid absorption and reduces serum folate levels.
- Colestipol: Reduces folic acid absorption and reduces serum folate levels.

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- Cycloserine: Reduces folic acid absorption and reduces serum folate levels.
- 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, sulfasalazine, pyrimethamine, triamterene, and trimethoprim.
- Isotretinoin: Reduced folate levels have occurred in some patients taking isotretinoin.
- Nonsteroidal Anti-Inflammatory Drugs (NSAIDs): NSAIDs have been shown to inhibit some folate dependant enzymes in laboratory experiments. NSAIDs include ibuprofen, naproxen, indomethacin and sulindac.
- Oral Contraceptives: Serum folate levels may be depressed by oral contraceptive therapy.
- Methylprednisone: Reduced serum folate levels have been noted after treatment with methylprednisolone.
- Pancreatic Enzymes: Reduced folate levels have occurred in some patients taking pancreatic extracts.
- Pentamidine: Reduced folate levels have been seen with prolonged intravenous pentamidine.
- Smoking and Alcohol: Reduced serum folate levels have been noted.
- Sulfasalazine: Inhibits the absorption and metabolism of folic acid.

#### **ADVERSE REACTIONS**

Allergic reactions have been reported following the use of both oral and parenteral folic acid, as well as the use of oral L-methylfolate.

#### **DOSAGE AND ADMINISTRATION**

The usual dose is 7.5 to 15 mg daily with or without food or as directed by a physician. L-methylfolate Calcium 7.5 mg tablets are available by prescription only.

#### **HOW SUPPLIED**

L-methylfolate Calcium 7.5 mg tablets are supplied in child-resistant bottles of 30 tablets (NDC# 42192-312-30).

Store at controlled room temperature 15° - 30°C (59° - 86°F) (See USP). Protect from light and moisture. Dispense product in original light-resistant container.

All prescription substitutions and/or recommendations using this product shall be made subject to state and federal statutes as applicable. Please note: this is not an Orange Book product and has not been subjected to FDA therapeutic equivalency or other equivalency testing. No representation is made as to generic status or bioequivalency. Each person recommending a prescription substitution using this product shall make such recommendations based on each such person's professional opinion and knowledge, upon evaluating the active ingredients, excipients, inactive ingredients and chemical information provided herein.

#### **MANUFACTURED FOR**

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