L-Methylfolate Calcium 7.5 mg

Tablets

Prescription Dietary Supplement

Product code* 44183-075-31 (30ct bottle / 30 tablets) Product code* 44183-075-90 (90ct bottle / 90 tablets)

-Methylfolate Calcium

patients with unique nutritional needs requiring increased folate levels. L-Methylfolate Calcium 7.5 mg should be administered under the supervision of a Each coated, round, blue tablet contains the following dietary ingredient: Supplement Facts **Supplement Facts** Serving Size 1 Tablet | Servings Per Container 30.

** Daily values not established for patients with uplque nutritional needs who are in need of supplementation as directed by a licensed medical practitioner

Other Ingredients: Citric Acid, Dicalcium Phosphate, FD&C Blue #2 Lake, Hypromellose, Magnesium Stearate, Microcrystalline Cellulose, Polyethylene Glycol, Polyvinyl Alcohol, Silicified Microcrystalline Cellulose, Talc, Titanium Dioxide and TriPotassium Citrate.

L-Methylfolate Calcium*, or 6(S)-5-MTHF-Ca

DESCRIPTION: L-Methylifolate Calcium 7.5 mg is an orally administered prescription dietary supplement specifically formulated for the dietary management of

FOLATE REGULATION: The term "folate" are B vitamins that include folic acid and any forms of active pteroylglutamates regardless of the reduction state of the molecule. Folates, or vitamin B9, are primarily hydrolyzed in the intestinal jejunum and the liver to the active circulating form of folate, I-methylfolate, with an Intermediate stable form, 5,10-methylenetetrahydrofolate.

Individuals with genetic polymorphorisms for the genes coding methylenetetrahydrofolate reductase (MTHFR) may not be capable of utilizing or metabolizing folic acid adequately for the vitamin Bix dependent methylation cycle.

Folicacid, including reduced forms' such as folinic acid, may obscure pernicious anemia above 0.1 mg doses, and must be administered under the supervision of

The 1971, 1972, 1973, 1980, 1984; 2000, and 2010 Federal Register Notices addressed this concern while establishing that increased folate was proper therapy in megaloblastic anemias - specifically where homogysteine levels were elevated or risk of neural tube defects (NTDs) was at issue. The Federal Register Notice of August 2, 1973 (38 FR 20750) specifically states that:

Dietary supplement preparations are available without a prescription (21:CFR 121.1134). Levels higher than dietary 2334-467 glassissupplement amounts are available only with a prescription.

it is not known whether or not i-methylfolate can obscure pemicious anemia above 0.1 mg doses, so caution is advised also with this form of folate.

Folicacid - including reduced forms, may be added to medical foods as defined in section 5(b)(3) of the Orphan Drug Act (21 USC 360ee(b)(3)), or to food (21 CFR

INDICATIONS AND USAGE: L-Methyliolate Calcium 7.5 mg is indicated for the distinct nutritional requirements of patients in need of dietary supplementation as determined by a licensed medical practitioner.

L-Methylfolate Calcium 7.5 mg should be administered under the supervision of a licensed medical practitioner.

CONTRAINDICATIONS: This product is contraindicated in patients with a known hypersensitivity to any of the ingredients.

WARNINGS: Caution is recommended in patients with a history of bipolar illness.

PRECAUTIONS: General: Foliate, when administered as a single agent in doses about 0.1 mg daily, may obscure the detection of vitamin B12 deficiency (specifically, the administration of folic acid may reverse the hematological manifestations of B12 deficiency, including permicious anemia, while not addressing the neurological manifestations).

Folate therapy alone is inadequate for treatment of a vitamin 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. L-Methylfolate Calcium 7.5 mg is not an antidepressant; however, folate has been shown to enhance antidepressant effects of known antidepressants. 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.

PATIENT INFORMATION: L-Methylfolate Calcium 7.5 mg is a prescription dietary supplement to be used only under licensed medical supervision.

MERCK EXHIBIT Replacement 2188 Gnosis v Merck & Cie IPR2013-00117

Praduct Code* 44183-075-31 (30ct borde)

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DRUG INTERACTIONS: Drugs which may interact with foliate Include:

- Antiepileptic drugs (AED): The AED class including, but not limited to, phenytoin, carbamazepine, primidone, valproic acid, fosphenytoin, valproate, 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 the AED in the blood and allowing breakthrough seizures to occur. Caution should be used when prescribing this product among patients who are receiving treatment with phenytoin and other
- 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.
 Cycloserine: Reduces folic acid absorption and reduces serum folate levels.
- . Dihydrofolate Reductase Inhibitors (DHFRI): DHFRIs block the conversion of folic acid to its active forms, and lower plasma and red blood cell folate levels. DHERIs include aminopterin, methorrexate, pyrimethamine, triamterene, and trimethoprim.
- Fluoxetine: Fluoxetine exerts a noncompetitive inhibition of the 5-methyltetrahydrofolate active transport in the intestine.
- Isotretinoin: Reduced folate levels have occurred in some patients taking isotretinoin.
- L-dopa, triamterene, coichicine, and trimethoprim may decrease plasma folate levels.
- . Nonsteroldal Ariti-Inflammatory Drugs (NSAIDs): NSAIDs have been shown to inhibit some folate dependent enzymes in laboratory experiments,
- NSAIDs include ibuprofen, naproxen, indomethacin and sulindac.
- · Oral Contraceptives: Serum folate levels may be depressed by oral contraceptive therapy.
- Methylprednisolone: Reduced serum folate levels have been noted after treatment with methylprednisolone.
- Pancreatic Enzymes: Reduced folate levels have occurred in some patients taking pancreatic extracts, such as pancreatin and pancrelipase.
- Pentamidine: Reduced folate levels have been seen with prolonged intravenous pentamidine.
- Pyrimethamine: High levels of folic acid may result in decreased serum levels of pyrimethamine.
- Smoking and Alcohol: Reduced serum folgte levels have been noted.
- Sulfasalazine: Inhibits the absorption and metabolism of folic acid. Metformin treatment in patients with type 2 diabetes decreases serum folate.
- · Warfarin can produce significant impairment in folate status after a 6-month therapy.

PREGNANCY and NURSING MOTHERS: L-Methylfolate Caldium 7.5 mg is not intended for use as a prenatal/postnatal multivitamin for lactaung and

nonlactating mothers. This product contains a B vitamin in reduced form. Talk with your medical practitioner before using if pregnant or lactating. ADVERSE REACTIONS: Allergic sensitization has been reported following both oral and parental administration of folic acid, and may possibly occur with other

DOSAGE AND ADMINISTRATION: The usual adult dose is 7.5 to 15 mg daily with or without food or as directed by a licensed medical practitioner.

ROW SUPPLIED: L-Methylfolate Calcium 7.5 mg tablets are coated, round, blue tablets debossed on one side with "MP7.5" ("7.5" underneath "MP"), and are supplied in bottles of 30 tablets and 90 tablets.

STORAGE: Store at controlled room temperature 15°-30°C (59°-86°F), [See USP], Protect from light and moisture. Dispense in a tight, light-resistant container.

KEEP THIS OUT OF REACH OF CHILDREN.

All prescriptions using this product shall be pursuant to state statutes as applicable. This is not an Orange Book product.

Call your medical practitioner about side effects. You may report side effects by calling 877-622-6836.

Product code* 44183-075-31 (30ct boutle / 30 tablets)

Product code 44183-075-90 (90ct bottle / 90 tablets)

Majoven Pharmaceuticals does not represent this product code to be National Drug Code (RINO) number. Instead, Maxoven has assigned a product code formatted according to standard industry practice to meet the formatting requirements of pharmacy and health insurance computer systems.

Prescription Dietary Supplement

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Manufactured for: Macoven Pharmaceuticals Magnolia, TX 77354 MADE IN CANADA

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.-Methylfolate Calcium 15 mg

LaMethylfolate Calcium 15 mg

Tablets

Prescription Dietary Supplement 90ct Bottle

DESCRIPTION: L-Methylfolate Calcium 15 mg is an orally administered prescription dietary supplement specifically formulated for the dietary management of patients with unique nutritional needs requiring increased foliate levels.

L-Methylfolate Calcium 15 mg should be administered under the supervision of a licensed medical practitioner.

Each coated, oval, orange tablet contains the following dietary ingredient:

Supplement Facts

Serving Size 1 Tablet Servings Per Containe

Amount Per Serving L-Methylfolate Calcium*, or 6(S)-5-MTHF-Ca 15 mg usavi ya buri et

shed for patients with unique nutritional needs who are in need of supplementation as directed by a licensed medical practiti Other Ingredients: Citric Acid, Dicalcium Phosphate, FD&C Yellow #5 Lake***, FD&C Yellow #6 Lake***, FD&C Red #40 Lake, Hypromeliose, Magnesium Stearate, Microcrystalline Cellulose, Rolyethylere Glycol, Polyvinyl Alcohol, Silicified Microcrystalline Cellulose, Tale, Titanium Dicylde, and Titanium Cellulose, Tale, Dioxide, and TriPotassium Citrate.

*** This product contains FD&C Yellow #5 Lake (tartrazine) and FD&C Yellow #6 Lake.

To Late REGULATION: The term "folate," are B vitamins that include folio acid and any forms of active pteroy(glutamates regardless of the reduction state of the molecule. Folates, or vitamin Bs, are primarily hydrolyzed in the intestinal jejunum and the liver to the active circulating form of folate. I-methyfolate, with an intermediate stable form, 5,10-methylenetetralydorfolate. Individuals with genetic polymorphorisms for the genes coding methylenetetrahydrofolate reductase (MTHFF) may not be capable of utilizing or metabolizing folio acid adequately for the vitamin Bry dependent methylation cycle.

Folic acid; including reduced forms such as folinic acid, may obscure permicious anemia above 0.1 mg doses, and must be administered under the supervision of a licensed medical practitioner.

The 1971, 1972, 1973, 1980, 1984, 2000; and 2010 Federal Register Notices addressed this concern while establishing that increased tolate was proper therapy in megacolastic anemias. "specifically where homocysteline levels were elevated or risk of neural tube defects (NTDs) was at issue." The Federal Register Notice of August 2, 1973 (38 FR 20750) specifically states that:

Dietary supplement preparations are available without a prescription (21 CFR 121.1134). Levels higher than dietary supplement amounts are available only with a prescription."

* It is not known whether or not 'methylifolate can obscure permisious anemia above 0.1 mg doses, so caution is advised also with this form of folate.

Folic acid including reduced forms; may be added to medical foods as defined in section 5(b)(3) of the Orphan Drug Act (21 USC 360ee(b)(3)), or to food (21 CFR 172:345).

INDICATIONS AND USAGE: L-Methylfolate Calcium 15 mg is indicated for the distinct nutritional requirements of patients in need of dietary supplementation as determined by a licensed medical practitioner.

L-Methytrolate Cacium 15 mg should be administered under the supervision of a licensed medical practitioner.

CONTRAINDICATIONS: This product is contraindicated in patients with a known hypersensitivity to any of the ingredients.

WARNINGS: Caution is recommended in patients with a history of bipolar illness.

WARMINES, Caution is recommended in patients with a history of bipolar illness.

PRECAUTIONS: General: Folate, when administered as a single agent in doses about 0.1 mg daily, may obscure the detection of vitamin 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).

Folate therapy, alone, is inadequate for treatment of a vitamin B₁₂ deficiency.

A major depressive episode may be the initial presentation of bipolar disorder. It is generally believed, (atthough not established in controlled trials) that treating such an enticed with an antidepressant alone may increase the likelihood of a precipitation of a mixed/manic episode in patients at risk for hipolar disorder. Likelihyfolate Calcium 15 mg is not an antidepressant; however, folate has been shown to enhance antidepressant effects of known antidepressants. Caution is recommended in patients with a history of bipolar disorder since mood elevation in this population is possibile.

This product contains FD&C Yellow #5 Lake (tartrazine) which may cause allergic-type reactions (including bronchial astirma) in certain susceptible persons. Although the overall incidence of FD&C Yellow #5 Lake (tartrazine) sensitivity in the general population is low, it is trequently seen in patients who also have aspirin hypersensitivity.

This product also contains FD&C Yellow #6 Lake.

PATIENT INFORMATION: L-Methyliolate Calcium 15 mg is a prescription dietary supplement to be used only under licensed medical

L-Methylfolate Calcium 15 mg

DRUG INTERACTIONS: Drugs which may interact with folate include:

- Äntteplieptic drugs (AED): The AED class including, but not limited to, phenytoin, carbamazegine, primidone, valprois acid, fosphenytoin, Valproate, phenobarbital and lamourgine have been shown to impair folate absorption and increase the metabolism of circulating tolate.
- Additionally, conclurrent use of bilineacing in taxe been associated with enhanced phenytoin metabolism, lowering the level of the AB in the blood and allowing breakthrough sitzures to occur. Caution should be used when prescribing this product among patients who are receiving reatment with binington and other articlonyulasmiss.

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

- Colestipic: Reduces foil: acid absorption and reduces serum foliate levels:

 Ovelosenne: Reduces foil: acid absorption and reduces serum foliate levels:

 Ovelosenne: Reduces foil: acid absorption and reduces serum foliate levels:

 Olimprofolate Reductase inhibition; (OHERN): DHERNE block the conversion of foil: acid to its active forms, and lower plasma and red blood cell foliate jevels. DHERNE included aniholotient, methotrecare, pyrimethamine, transferene, and trimethoprim.

 Fluoxetine: Fluoxetine exerts a reprompetitive inhibition of the 5-methylitetrahydrofolate active transport in the intestine.

 Indicate Marketene exerts a reprompetitive inhibition of the 5-methylitetrahydrofolate active transport in the intestine.

- L-dopa, triamterene, colohicine, and trimethoprim may decrease plasma folate levels.
 Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)-NSAIDs have been shown to Inhibit some folate dependent enzymes in laboratory. Notice toward return appropriate properties and sulfidate.
 Notice include ibuprolen, naproken, indometherin and sulfidate.
 Oral Contraceptives: Serum foldel levels may be depressed by oral contraceptive therapy.
 Nethylprednisolonic. Reduced setrum folder levels may be depressed by oral contraceptive therapy.
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- Panticiatific Enzymes: Reduced felate levels have occurred in some patients taking pancreatic extracts, such as pancreatin and pancretipase.

 Pantimidinia: Reduced folate levels have been seen with protonged intravenous pentamidine.
- Pyrimethamine: High levels of folic acid may result in decreased serum levels of pyrimethamine.
- Smoking and Alcohol: Reduced serum folde levels have been noted.
 Surfassization: Inhibits the absorption and metabolism of titlic acid.
- Mettorfinir treatment in patients with type 2 diabetes decreases serum totate.
 Wartathi can produce significant impairment in folate status after a 6-houth therapy.

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PRESHARCY and NURSING WOTHERS: I hebryfrotate Calcium's fing is noblintended for use as a prenatal/postnatal multivitamin for lacitating and nonlactating mothers. This product contain a 8 viramin in reduced form. Talk with your medical practitioner before using if pregrant or lactating.**

AVERSE REACTIONS (Alergic sensitization flas been reported following both oral and parental administration of folic acid, and may possibly occur with other forms of foliate.

DOSAGE AND ADMINISTRATION. The usual adult dose is 15 mg daily with or without food or as directed by a licensed medical practitioner.

STORAGE: Store at controlled room temperature 15-30°C (69°-86°F). [See USF]. Protect from light and moisture. Dispense in a tight, "light-resistant container."

light-resistant container.

How Supplies: I. Methyltolate (alicium 15 mg tablets are coated, oval, orange tablets debossed on one side with "MP 15", and are supplied in porties of 90 tablets. KEEP THIS OUT OF REACH OF CHILDREN.

All prescriptions using this product shall be pursuant to state statutes as applicable. This is not an Orange Book product.

Call your medical practitioner about side effects. You may report side effects by calling 877-822-8836. Product code 1 44183-150-90 Start of the Stronger of State Williams la contant de la

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Prescription Dietary Supplement

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