DESCRIPTION: L-Methylfolate Calcium 7.5 mg is an orally administered prescription dietary supplement specifically formulated for the dietary management of patients with unique nutritional needs requiring increased folate levels.

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

Each coated, round, blue-tablet contains the following dietary ingredient:

Supplement Facts

Serving Size 1 Tablet
Servings Per Container 90

	Amount Per Serving	% Daily Value
L-Methylfolate Calcium*, or 6(S)-5-MTHF-Ca	7.5 mg	**

*contains less than 1% d-methylfolate.
**Daily Value not established for patients with unique nutritional needs who are in need of supplementation as directed by a licensed medical practitioner

Other ingredients: See insert for more information. Rev. 1/2012

VIRTUS PHARMACEUTICALS

NDC† 76439-206-90

L-Methylfolate Calcium 7.5 mg

Prescription Dietary Supplement

℞

90 Tablets

Made in USA

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.

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.

If you are pregnant or nursing a baby, seek a health professional.

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 (813) 283-1344.

NDC† 76439-206-90

†see insert for more information on NDCs.

Manufactured for: Virtus Pharmaceuticals, LLC Tampa, FL 33619

Lot No:

Exp Date:

N 3 76439 20690 1

NDC† 76439-206-30 (30 ct. bottle / 30 tablets)
NDC† 76439-206-90 (90 ct. bottle / 90 tablets)

L-Methylfolate Calcium 7.5 mg Tablets

℞

Prescription Dietary Supplement

DESCRIPTION: L-Methylfolate Calcium 7.5 mg is an orally administered prescription dietary supplement specifically formulated for the dietary management of patients with unique nutritional needs requiring increased folate levels.

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

Each coated, round, blue tablet contains the following dietary ingredient:

Supplement Facts

Serving Size: 1 tablet Servings per container: 30 (NDC† 76439-206-30)
Servings per container: 90 (NDC† 76439-206-90)

Amount Per Serving	% Daily Value
L-Methylfolate Calcium*, or 6(S)-5-MTHF-Ca ..... 7.5 mg	

*contains less than 1% d-methylfolate.
**Daily Value not established for patients with unique nutritional needs who are in need of supplementation as directed by a licensed medical practitioner.

Other ingredients: Dicalcium Phosphate, Microcrystalline Cellulose, FD&C Blue #2, Titanium Dioxide, Modified Cellulose, Croscarmellose Sodium, Stearic Acid, Magnesium Stearate, Silicon Dioxide, Polyethylene Glycol and Food Glaze.

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 B_9, are primarily hydrolyzed in the intestinal jejunum and the liver to the active circulating form of folate, L-methylfolate, with an intermediate stable form, 5,10-methylenetetrahydrofolate.

Individuals with genetic polymorphisms for the genes coding methylenetetrahydrofolate reductase (MTHFR) may not be capable of utilizing or metabolizing folic acid adequately for the vitamin B_{12} dependent methylation cycle.

Folic acid, including reduced forms‡ such as folinic acid, may obscure pernicious 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 folate was proper therapy in megaloblastic anemias - specifically where homocysteine 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 l-methylfolate can obscure pernicious 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 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: Folate, when administered as a single agent in doses about 0.1 mg daily, may obscure the detection of vitamin B_{12} deficiency (specifically, the administration of folic acid may reverse the hematological manifestations of B_{12} deficiency, including pernicious anemia, while not addressing the neurological manifestations).

Folate therapy alone is inadequate for treatment of a vitamin B_{12} 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.

DRUG INTERACTIONS: Drugs which may interact with folate 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 anticonvulsants.
- 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 (DHFR): DHFRs block the conversion of folic acid to its active forms, and lower plasma and red blood cell folate levels. DHFRs include aminopterin, methotrexate, 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, colchicine, and trimethoprim may decrease plasma folate levels.
- Nonsteroidal Anti-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 administration of pentamidine.
- Pyrimethamine: High levels of folic acid may result in decreased serum levels of pyrimethamine
- Smoking and Alcohol: Reduced serum folate 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.
- Folinic acid may enhance the toxicity of fluorouracil.
- Concurrent administration of chloramphenicol and folinic acid in folate-deficient patients may result in antagonism of the haematopoietic response to folates.
- Caution should be exercised with the concomitant use of folinic acid and trimethoprim-sulfamethoxazole for the acute treatment of *Pneumocystis carinii* pneumonia in patients with HIV infection as it is associated with increased rates of treatment failure and mortality in a placebo controlled study.

PREGNANCY and NURSING MOTHERS: L-Methylfolate Calcium 7.5 mg is not intended for use as a prenatal/postnatal multivitamin for lactating and non-lactating 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 forms of folate.

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.

HOW SUPPLIED: L-Methylfolate Calcium 7.5 mg tablets are coated, round, blue tablets debossed "BP" on top and "500" on bottom, and are supplied in bottles of 30 tablets and 90 tablets.

NDC† 76439-**206**-30 (30 ct. bottle / 30 tablets)
NDC† 76439-**206**-90 (90 ct. bottle / 90 tablets)

†These products are dietary supplements that – due to increased folate levels (8/2/73 38 FR 20750), require an Rx on the label because of increased risk associated with masking of B_{12} deficiency. As such, this product requires licensed medical supervision, an Rx status, and a National Drug Code (NDC) as required by pedigree reporting requirements.

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 813-283-1344.

L-Methylfolate Calcium 7.5 mg Tablets

℞

Prescription Dietary Supplement

Manufactured for:
Virtus Pharmaceuticals, LLC
Tampa, FL 33619
www.VirtusRX.com
MADE IN USA

VIRTUS PHARMACEUTICALS

Rev. 12/2012

L-Methylfolate Calcium 7.5 mg Tablets ℞ 76439-206-30 (30 ct. bottle / 30 tablets) 76439-206-90 (90 ct. bottle / 90 tablets)