

**L-METHYLFOLATE CALCIUM- levomefolate calcium tablet, coated**  
**Virtus Pharmaceuticals**

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**L-METHYLFOLATE CALCIUM 7.5mg Tablets**  
**L-METHYLFOLATE CALCIUM 15mg Tablets**

**DESCRIPTION**

L-METHYLFOLATE CALCIUM Tablets is a medical food dispensed by prescription for the clinical dietary management of the metabolic imbalances associated with depression and schizophrenia. Use under medical supervision.

Each L-METHYLFOLATE CALCIUM 7.5mg tablet contains 7.5 mg of L-METHYLFOLATE CALCIUM

Each L-METHYLFOLATE CALCIUM 15mg tablet contains 15mg of L-METHYLFOLATE CALCIUM .

**L-METHYLFOLATE CALCIUM Tablets 7.5mg Dietary Ingredients**

Dibasic Calcium Phosphate Dihydrate, Silicified Microcrystalline Cellulose 90, Silicified Microcrystalline Cellulose HD 90, Opadry II Blue 85F90748 (Polyvinyl Alcohol, Titanium Dioxide [color], PEG 3350, Talc and FD&C Blue #2[color]), L-METHYLFOLATE CALCIUM, Magnesium Stearate (Vegetable Source), and Carnauba Wax.

L-METHYLFOLATE CALCIUM 7.5mg tablets do not contain sugar, lactose, yeast or gluten.

**L-METHYLFOLATE CALCIUM 15mg Tablets Dietary Ingredients**

Dibasic Calcium Phosphate Dihydrate, Silicified Microcrystalline Cellulose 90, Opadry II Orange 85F43102, (Polyvinyl Alcohol, PEG 3350, Talc, Titanium Dioxide [color], FD&C Yellow #6[color], FD&C Yellow #5[color], FD&C Red #40[color] and FD&C Blue #2[color]), L-METHYLFOLATE CALCIUM, Magnesium Stearate (Vegetable Source), and Carnauba Wax.

L-METHYLFOLATE CALCIUM 15mg tablets do not contain sugar, lactose, yeast or gluten.

Medical foods are intended for a patient who has a limited or impaired capacity to ingest, digest, absorb, or metabolize ordinary foodstuffs or certain nutrients, or who has other special medically determined nutrient requirements, the dietary management of which cannot be achieved by the modification of the normal diet alone.<sup>1</sup> This product is not an Orange Book product.

**L-METHYLFOLATE CALCIUM Tablets is a medical food dispensed by prescription.**

**CLINICAL PHARMACOLOGY**

L-METHYLFOLATE CALCIUM Tablets is a medical food, which consists of a proprietary biologically active folate, derived from food sources.

**INDICATIONS AND USAGE**

**ADJUNCTIVE USE IN MAJOR DEPRESSIVE DISORDER** L-METHYLFOLATE CALCIUM Tablets is indicated for the distinct nutritional requirements of individuals who have suboptimal L-METHYLFOLATE CALCIUM Tablets levels 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.<sup>2-5</sup>

**ADJUNCTIVE USE IN SCHIZOPHRENIA** L-METHYLFOLATE CALCIUM Tablets is indicated for

the distinct nutritional requirements of individuals who have or are at risk for hyperhomocysteinemia and have schizophrenia who present with negative symptoms and/or cognitive impairment, with particular emphasis as an adjunctive support for individuals who have stabilized on antipsychotics.<sup>2</sup> L-METHYLFOLATE CALCIUM Tablets is indicated regardless of MTHFR C677T polymorphism genotype.<sup>6</sup>

## CONTRAINDICATIONS

L-METHYLFOLATE CALCIUM Tablets is contraindicated in patients with known hypersensitivity to any of the components contained in this product.

## PRECAUTIONS

### General

Folic acid, when administered in daily doses above 0.1mg, 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 CALCIUM Tablets may be less likely than folic acid to mask vitamin B<sub>12</sub> deficiency.<sup>7,8</sup> Folate therapy alone is inadequate for the treatment of a B<sub>12</sub> 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 Tablets is not an antidepressant; however, 5-MTHF has been shown to enhance antidepressant effects of known antidepressants.<sup>2</sup> 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 Tablets is a medical food<sup>1</sup> for use under medical supervision and direction.

**L-METHYLFOLATE CALCIUM Tablets is a medical food dispensed by prescription.**

### Interaction with Drugs

Before using this product, tell your doctor or pharmacist of all the products you use. Keep a list of all 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 L-METHYLFOLATE CALCIUM Tablets.

L-METHYLFOLATE CALCIUM Tablets contains folate, which may have interactions 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.<sup>9,10,12,15</sup>
- Capecitabine: Folinic acid (5-formyltetrahydrofolate) may increase the toxicity of Capecitabine.<sup>11</sup>
- 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.<sup>12</sup>
- Fluoxetine: Fluoxetine exerts a noncompetitive inhibition of the 5-methyltetrahydrofolate active transport in the intestine.<sup>13</sup>

- Isotretinoin: Reduced folate levels have occurred in some patients taking isotretinoin,<sup>14</sup>
- 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.<sup>12</sup>
- Oral Contraceptives: Serum folate levels may be depressed by oral contraceptive therapy. <sup>12</sup>
- Methylprednisolone: Reduced serum folate levels have been noted after treatment with methylprednisolone. <sup>12</sup>
- Pancreatic Enzymes: Reduced folate levels have occurred in some patients taking pancreatic extracts. <sup>12</sup>
- Pentamidine: Reduced folate levels have been seen with prolonged intravenous pentamidine. <sup>12</sup>
- Metformin treatment in patients with type 2 diabetes decreases serum folate.<sup>16,17</sup>
- Warfarin can produce significant impairment in folate status after a 6-month therapy.<sup>18</sup>

## ADVERSE REACTIONS

Allergic reactions have been reported following the use of oral L-METHYLFOLATE CALCIUM Tablets.

## DOSAGE AND ADMINISTRATION

The usual adult dose is 7.5mg to 15mg given daily with or without food or as directed under medical supervision.

## HOW SUPPLIED

**L-METHYLFOLATE CALCIUM Tablets is a medical food dispensed by prescription**

**7.5mg** Bottle of 30 Product Code # 76439-359-30<sup>1</sup>

Use under medical/physician supervision.

Bottle of 90 Product Code # 76439-359-90<sup>1</sup>

Use under medical/physician supervision.

A light blue, round, coated, tablet debossed on one side with "V359" and blank on the other.

**15mg** Bottle of 90 Product Code # 76439-358-90<sup>1</sup>

Use under medical/physician supervision.

An orange, oval, coated, caplet debossed on one side with "V358" and blank on the other.

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<sup>1</sup> Virtus Pharmaceuticals, LLC does not represent these product codes to be National Drug Codes (NDC). Product codes are formatted according to standard industry practice, to meet the formatting requirements of pharmacy and health insurance computer systems

## Storage

Store at controlled room temperature 15°C to 30°C (59°F to 86°F) (See USP). Protect from heat, light and moisture.

## PATENTS

Some or all of the following patents may apply: U.S. Patent No. 6,011,040 U.S. Patent No. 6,441,168B1 and other pending patent applications

## REFERENCES

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11. Capecitabine Package Insert; Roche Laboratories, 2000
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14. Chanson A, et al. JEADV 2008, 22:94-100
15. Tatum IV W et al. Arch Intern Med. 2004; 164: 137-45.
16. Wulffele MG, et al. Journal of Internal Medicine 2003; 254: 455-463.
17. Desouza C, et al. Drugs 2002; 62(4): 605-16.
18. Sobczyriska-Malefora A et al. Blood Coagul Fibrinolysis 2009 Jun; 20(4):297-302

Manufactured for:

**Virtus Pharmaceuticals, LLC**  
**Tampa, FL 33619**

PC0294-00

Revised 11/14

## PRINCIPAL DISPLAY PANEL - 15 mg Tablet Bottle Label

**VIRTUS**  
PHARMACEUTICALS

76439-358-90

**L-Methylfolate**  
**Calcium**  
**15 mg**

**R<sub>x</sub>**  
**90 Tablets**

Made in USA

**Description:**  
Each L-Methylfolate Calcium 15mg orange, oval, coated tablet contains 15mg of L-methylfolate.

**Ingredients:** Dibasic Calcium Phosphate Dihydrate, Silicified Microcrystalline Cellulose 90, Opadry II Orange 85F43102, (Polyvinyl Alcohol), PEG 3350, Talc, Titanium Dioxide [color], FD&C Yellow #6 [color], FD&C Yellow #5 [color], FD&C Red #40 [color] and FD&C Blue #2 [color], L-methylfolate Calcium, Magnesium Stearate (Vegetable Source), and Carnauba Wax, Sugar, Lactose, Yeast & Gluten Free.

**DOSAGE AND ADMINISTRATION:** The usual adult dose is 15 mg daily with or without food or as directed by a licensed medical practitioner. This product has been manufactured in a facility that also manufactures products containing milk and soy. Individuals with allergic tendencies to these substances should use discretion.

**Pharmacists:** L-METHYLFOLATE CALCIUM 15mg Tablets is a medical food dispensed by prescription for the clinical dietary management of the metabolic imbalances associated with depression and schizophrenia. [Use under medical supervision] *Rev. 11/14*

**VIRTUS PHARMACEUTICALS**  
76439-358-90

**L-Methylfolate Calcium 15 mg**

**Rx 90 Tablets** Made in USA

**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, ask 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.**

Manufactured for: Virtus Pharmaceuticals LLC, Tampa, FL 33619

Lot No:                      Exp:

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PC0286-00

**PRINCIPAL DISPLAY PANEL - 7.5 mg Tablet Bottle Label**

**VIRTUS  
PHARMACEUTICALS**

76439-359-90

**L-Methylfolate  
Calcium  
7.5 mg**

**Rx  
90 Tablets**

Made in USA

**Description:**  
Each L-Methylfolate Calcium 7.5mg light blue colored, coated, round tablet contains 7.5mg of L-methylfolate.

**Ingredients:** Dibasic Calcium Phosphate Dihydrate, Silicified Microcrystalline Cellulose 90, Silicified Microcrystalline Cellulose HD 90, Opadry II Blue 85F90748 (Polyvinyl Alcohol), Titanium Dioxide [color], PEG 3350, Talc and FD&C Blue #2 [color], L-methylfolate Calcium, Magnesium Stearate (Vegetable Source), and Carnauba Wax, Sugar, Lactose, Yeast & Gluten Free.

**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. This product has been manufactured in a facility that also manufactures products containing milk and soy. Individuals with allergic tendencies to these substances should use discretion.

**Pharmacists:** L-METHYLFOLATE CALCIUM 7.5mg Tablets is a medical food dispensed by prescription for the clinical dietary management of the metabolic imbalances associated with depression and schizophrenia. [Use under medical supervision]. *Rev. 11/14*

**VIRTUS PHARMACEUTICALS**  
76439-359-90


**L-Methylfolate Calcium 7.5 mg**

**Rx 90 Tablets** Made in USA

**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, ask 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 or 1-888-848-3593.**

Manufactured for: Virtus Pharmaceuticals LLC, Tampa, FL 33619

Lot No:                      Exp:

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PC0286-01

**L-METHYLFOLATE CALCIUM**

levomefolate calcium tablet, coated

**Product Information**

<b>Product Type</b>	MEDICAL FOOD	<b>Item Code (Source)</b>	NHRIC:76439-358
<b>Route of Administration</b>	ORAL		

**Active Ingredient/Active Moiety**

Ingredient Name	Basis of Strength	Strength
LEVOMEFOLATE CALCIUM (UNII: A9R10K3F2F) (LEVOMEFOLIC ACID - UNII:8S95DH25XC)	LEVOMEFOLATE CALCIUM	15 mg

**Inactive Ingredients**

Ingredient Name	Strength
CALCIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: O7TSZ97GEP)	
POLYVINYL ALCOHOL (UNII: 532B59J990)	
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P)	
TALC (UNII: 7SEV7J4R1U)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
FD&C YELLOW NO. 6 (UNII: H77VEI93A8)	
FD&C YELLOW NO. 5 (UNII: I753WB2F1M)	
FD&C RED NO. 40 (UNII: WZB9127XOA)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CARNAUBA WAX (UNII: R12CBM0EIZ)	

**Product Characteristics**

Color	ORANGE	Score	no score
Shape	OVAL (caplet)	Size	24mm
Flavor		Imprint Code	V358
Contains			

**Packaging**

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NHRIC:76439-358-90	90 in 1 BOTTLE		

**Marketing Information**

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
MEDICAL FOOD		01/08/2015	

**L-METHYLFOLATE CALCIUM**

levomefolate calcium tablet, coated

**Product Information**

Product Type	MEDICAL FOOD	Item Code (Source)	NHRIC:76439-359
Route of Administration	ORAL		

**Active Ingredient/Active Moiety**

Ingredient Name	Basis of Strength	Strength
LEVOMEFOLATE CALCIUM (UNII: A9R10K3F2F) (LEVOMEFOLIC ACID - UNII:8S95DH25XC)	LEVOMEFOLATE CALCIUM	7.5 mg

**Inactive Ingredients**

Ingredient Name	Strength
CALCIUM PHOSPHATE, DIBASIC, DIHYDRATE (UNII: O7TSZ97GEP)	
POLYVINYL ALCOHOL (UNII: 532B59J990)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
POLYETHYLENE GLYCOL 3350 (UNII: G2M7P15E5P)	
TALC (UNII: 7SEV7J4R1U)	
FD&C BLUE NO. 2 (UNII: L06K8R7DQK)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
CARNAUBA WAX (UNII: R12CBM0EIZ)	

**Product Characteristics**

Color	BLUE (Light blue)	Score	no score
Shape	ROUND	Size	14mm
Flavor		Imprint Code	V359
Contains			

**Packaging**

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NHRIC:76439-359-30	30 in 1 BOTTLE		
2	NHRIC:76439-359-90	90 in 1 BOTTLE		

**Marketing Information**

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
MEDICAL FOOD		02/09/2015	

**Labeler** - Virtus Pharmaceuticals (969483143)

Revised: 9/2015

Virtus Pharmaceuticals