

VITAMIN D - ergocalciferol capsule
Aphena Pharma Solutions - Tennessee, LLC

DESCRIPTION

Ergocalciferol capsules, USP, is a synthetic calcium regulator for oral administration.

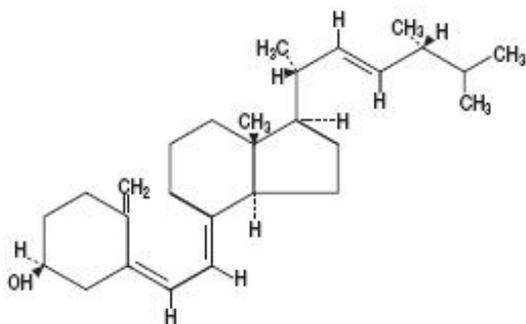
Ergocalciferol is a white, colorless crystal, insoluble in water, soluble in organic solvents, and slightly soluble in vegetable oils. It is affected by air and by light. Ergosterol or provitamin D₂ is found in plants and yeast and has no antirachitic activity.

There are more than 10 substances belonging to a group of steroid compounds, classified as having vitamin D or antirachitic activity.

One USP unit of vitamin D₂ is equivalent to one International Unit (IU), and 1 mcg of vitamin D₂ is equal to 40 IU.

Each capsule contains 1.25 mg (50,000 USP Units vitamin D) of ergocalciferol, USP, in an edible vegetable oil.

Ergocalciferol, also called vitamin D₂, is 9,10-secoergosta-5,7,10 (19),22-tetraen-3-ol,(3 β ,5Z,7E,22E)-;(C₂₈H₄₄O) with a molecular weight of 396.65, and has the following structural formula:



The soft gelatin capsule and imprinting ink contain: ammonium hydroxide, butyl alcohol, D&C Yellow No. 10, FD&C Blue No. 1, gelatin, glycerin, isopropyl alcohol, propylene glycol, purified water, shellac glaze, simethicone, soybean oil, and titanium dioxide.

CLINICAL PHARMACOLOGY

The *in vivo* synthesis of the major biologically active metabolites of vitamin D occurs in two steps. The first hydroxylation of ergocalciferol takes place in the liver (to 25-hydroxyvitamin D) and the second in the kidneys (to 1,25-dihydroxyvitamin D). Vitamin D metabolites promote the active absorption of calcium and phosphorus by the small intestine, thus elevating serum calcium and phosphate levels sufficiently to permit bone mineralization. Vitamin D metabolites also mobilize calcium and phosphate from bone and probably increase the reabsorption of calcium and perhaps also of phosphate by the renal tubules.

There is a time lag of 10 to 24 hours between the administration of vitamin D and the initiation of its action in the body due to the necessity of synthesis of the active metabolites in the liver and kidneys. Parathyroid hormone is responsible for the regulation of this metabolism in the kidneys.

INDICATIONS AND USAGE

Ergocalciferol Capsules, USP are indicated for use in the treatment of hypoparathyroidism, refractory rickets, also known as vitamin D resistant rickets, and familial hypophosphatemia.

CONTRAINDICATIONS

Ergocalciferol Capsules, USP are contraindicated in patients with hypercalcemia, malabsorption syndrome, abnormal sensitivity to the toxic effects of vitamin D, and hypervitaminosis D.

WARNINGS

Hypersensitivity to vitamin D may be one etiologic factor in infants with idiopathic hypercalcemia. In these cases vitamin D must be strictly restricted.

Keep out of the reach of children.

PRECAUTIONS

General

Vitamin D administration from fortified foods, dietary supplements, self-administered and prescription drug sources should be evaluated. Therapeutic dosage should be readjusted as soon as there is clinical improvement. Dosage levels must be individualized and great care exercised to prevent serious toxic effects. IN VITAMIN D RESISTANT RICKETS THE RANGE BETWEEN THERAPEUTIC AND TOXIC DOSES IS NARROW. When high therapeutic doses are used progress should be followed with frequent blood calcium determinations.

In the treatment of hypoparathyroidism, intravenous calcium, parathyroid hormone, and/or dihydrotachysterol may be required.

Maintenance of a normal serum phosphorus level by dietary phosphate restriction and/or administration of aluminum gels as intestinal phosphate binders in those patients with hyperphosphatemia as frequently seen in renal osteodystrophy is essential to prevent metastatic calcification.

Adequate dietary calcium is necessary for clinical response to vitamin D therapy.

Protect from light.

Drug Interactions

Mineral oil interferes with the absorption of fat-soluble vitamins, including vitamin D preparations.

Administration of thiazide diuretics to hypoparathyroid patients who are concurrently being treated with ergocalciferol may cause hypercalcemia.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No long-term animal studies have been performed to evaluate the drug's potential in these areas.

Pregnancy Category C

Animal reproduction studies have shown fetal abnormalities in several species associated with hypervitaminosis D. These are similar to the supravalvular aortic stenosis syndrome described in infants by Black in England (1963). This syndrome was characterized by supravalvular aortic stenosis, elfin facies, and mental retardation. For the protection of the fetus, therefore, the use of vitamin D in excess of the recommended dietary allowance during normal pregnancy should be avoided unless, in the judgment of the physician, potential benefits in a specific, unique case outweigh the significant hazards involved. The safety in excess of 400 USP Units of vitamin D daily during pregnancy has not been established.

Nursing Mothers

Caution should be exercised when ergocalciferol is administered to a nursing woman. In a mother given large doses of vitamin D, 25-hydroxycholecalciferol appeared in the milk and caused hypercalcemia in her child. Monitoring of the infant's serum calcium concentration is required in that case (Goldberg, 1972).

Pediatric Use

Pediatric doses must be individualized (see **DOSAGE AND ADMINISTRATION**).

Geriatric Use

Clinical studies of ergocalciferol did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. A few published reports have suggested that the absorption of orally administered vitamin D may be attenuated in elderly compared to younger individuals. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

ADVERSE REACTIONS

Hypervitaminosis D is characterized by effects on the following organ system:

Renal: Impairment of renal function with polyuria, nocturia, polydipsia, hypercalciuria, reversible azotemia, hypertension, nephrocalcinosis, generalized vascular calcification, or irreversible renal insufficiency which may result in death.

CNS: Mental retardation.

Soft Tissues: Widespread calcification of the soft tissues, including the heart, blood vessels, renal tubules, and lungs.

Skeletal: Bone demineralization (osteoporosis) in adults occurs concomitantly.

Decline in the average rate of linear growth and increased mineralization of bones in infants and children (dwarfism), vague aches, stiffness, and weakness.

Gastrointestinal: Nausea, anorexia, constipation.

Metabolic: Mild acidosis, anemia, weight loss.

OVERDOSAGE

The effects of administered vitamin D can persist for two or more months after cessation of treatment.

Hypervitaminosis D is characterized by:

1. Hypercalcemia with anorexia, nausea, weakness, weight loss, vague aches and stiffness, constipation, mental retardation, anemia and mild acidosis.
2. Impairment of renal function with polyuria, nocturia, polydipsia, hypercalciuria, reversible azotemia, hypertension, nephrocalcinosis, generalized vascular calcification, or irreversible renal insufficiency which may result in death.
3. Widespread calcification of the soft tissues, including the heart, blood vessels, renal tubules, and lungs. Bone demineralization (osteoporosis) in adults occurs concomitantly.
4. Decline in the average rate of linear growth and increased mineralization of bones in infants and children (dwarfism).

The treatment of hypervitaminosis D with hypercalcemia consists in immediate withdrawal of the vitamin, a low calcium diet, generous intake of fluids, along with symptomatic and supportive treatment. Hypercalcemic crisis with dehydration, stupor, coma, and azotemia requires more vigorous treatment. The first step should be hydration of the patient. Intravenous saline may quickly and significantly increase urinary calcium excretion. A loop diuretic (furosemide or ethacrynic acid) may be given with the saline infusion to further increase renal calcium excretion. Other reported therapeutic measures include dialysis or the administration of citrates, sulfates, phosphates, corticosteroids, EDTA (ethylenediaminetetraacetic acid), and mithramycin via appropriate regimens. With appropriate therapy, recovery is the usual outcome when no permanent damage has occurred. Deaths via renal or cardiovascular failure have been reported.

The LD₅₀ in animals is unknown. The toxic oral dose of ergocalciferol in the dog is 4 mg/kg.

DOSAGE AND ADMINISTRATION

THE RANGE BETWEEN THERAPEUTIC AND TOXIC DOSES IS NARROW.

Vitamin D Resistant Rickets: 12,000 to 500,000 USP units daily.

Hypoparathyroidism: 50,000 to 200,000 USP units daily concomitantly with calcium lactate 4g, six times per day.

DOSAGE MUST BE INDIVIDUALIZED UNDER CLOSE MEDICAL SUPERVISION.

Calcium intake should be adequate. Blood calcium and phosphorus determinations must be made every 2 weeks or more frequently if necessary. X-rays of the bones should be taken every month until condition is corrected and stabilized.

HOW SUPPLIED

Repackaged by Aphenia Pharma Solutions - TN.
See ***Repackaging Information*** for available configurations.



Each softgel capsule contains Vitamin D (Ergocalciferol) 1.25 mg equivalent to 50,000 USP Units. The capsules are clear, dark green and oblong shaped, imprinted with "136" in white ink and are available as follows:

NDC 57664-136-85 Bottles of 50
NDC 57664-136-88 Bottles of 100
NDC 57664-136-18 Bottles of 1000

Store at 20° - 25°C (68° - 77°F) excursions permitted between 15° - 30°C (59 - 86°F). (See USP Controlled Room Temperature). Protect from light and moisture.

Dispense in a tight, light-resistant container as defined in the USP.

Distributed by:

Caraco Pharmaceutical Laboratories Ltd.

Detroit, MI 48202

Affiliate of

Sun Pharmaceutical Industries, Inc.

Stock #6142T01

Issued December 2008

Repackaging Information

Please reference the **How Supplied** section listed above for a description of individual tablets or capsules. This drug product has been received by Aphenia Pharma - TN in a manufacturer or distributor packaged configuration and repackaged in full compliance with all applicable cGMP regulations. The package configurations available from Aphenia are listed below:

Count	1.25mg
3	43353-828-03
4	43353-828-04

Store between 20°-25°C (68°-77°F). See USP Controlled Room Temperature. Dispense in a tight light-resistant container as defined by USP. Keep this and all drugs out of the reach of children.

Repackaged by:



Cookeville, TN 38506

20130719AW

PRINCIPAL DISPLAY PANEL - 1.25mg

NDC 43353-828 - **Ergocalciferol (50,000 USP Units Vitamin D) 1.25mg** - Rx Only

The principal display panel is a rectangular label with a white background and black text. At the top center, it reads "NDC # 43353-0828-03" and "Ergocalciferol (50,000 USP Units vitamin D)". Below this, the dosage and quantity "1.25mg 3 Capsule" are prominently displayed. The label includes storage instructions: "Store between 20-25 degrees C (68-77 degrees F). See USP Controlled Room Temperature. Dispense in a tight light-resistant container as defined by USP. Keep this and all drugs out of the reach of children." The manufacturer information is "Mfg. By: Pharmaceuticals International, Inc. Hunt Valley, MD". The repackager information is "Repackaged by Aphenia Pharma Cookeville, TN 38506". On the left side, there is a vertical barcode with the text "Ergocalciferol (50,000 USP Units vitamin D)", "1.25mg 3 Capsule", and "N 43353-0828-03". On the right side, there is another vertical barcode with the text "Batch:", "Exp:", "Lot:", "RX Only", and "N 43353-0828-03". At the bottom center, the text "Ergocalciferol (50,000 USP Units vitamin D) 1.25mg 3 Capsule" is repeated.

VITAMIN D

ergocalciferol capsule

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:43353-828(NDC:57664-136)
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
ERGOCALCIFEROL (UNII: VS041H42XC) (ERGOCALCIFEROL - UNII:VS041H42XC)	ERGOCALCIFEROL	1.25 mg

Inactive Ingredients

Ingredient Name	Strength
AMMONIA (UNII: 5138Q19F1X)	
BUTYL ALCOHOL (UNII: 8PJ61P6TS3)	
D&C YELLOW NO. 10 (UNII: 35SW5USQ3G)	
FD&C BLUE NO. 1 (UNII: HBR47K3TBD)	
GELATIN (UNII: 2G86QN327L)	
GLYCERIN (UNII: PDC6A3C0OX)	
ISOPROPYL ALCOHOL (UNII: ND2M416302)	
PROPYLENE GLYCOL (UNII: 6DC9Q167V3)	
WATER (UNII: 059QF0KO0R)	
SHELLAC (UNII: 46N107B71O)	
DIMETHICONE (UNII: 92RU3N3Y1O)	
SOYBEAN OIL (UNII: 241ATL177A)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	

Product Characteristics

Color	GREEN (dark green)	Score	no score
Shape	OVAL (oblong)	Size	5mm
Flavor		Imprint Code	136
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:43353-828-03	3 in 1 BOTTLE, PLASTIC		
2	NDC:43353-828-04	4 in 1 BOTTLE, PLASTIC		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA040865	03/15/2010	

Labeler - Aphenia Pharma Solutions - Tennessee, LLC (128385585)

Establishment

Name	Address	ID/FEI	Business Operations
Aphena Pharma Solutions - Tennessee, LLC		128385585	Repack(43353-828)

Revised: 7/2013

Aphena Pharma Solutions - Tennessee, LLC