PRESCRIBING INFORMATION

PrSANDOZ D 10 000

Vitamin D_3 (Cholecalciferol) capsules

Capsules, 10,000 IU, Oral

Vitamin D product

Sandoz Canada Inc.
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Vitamin D_3 (Cholecalciferol) capsules

Therapeutic Classification

Vitamin D Product

Pharmacology

Vitamin D is a fat-soluble vitamin that helps regulate serum calcium and phosphorous concentrations by enhancing the efficiency of the small intestine to absorb these minerals from the diet. Vitamin D has two main forms: cholecalciferol (Vitamin D_3), and ergocalciferol (Vitamin D_2).
One microgram (mcg) is equivalent to 40 IU of vitamin D activity. Vitamin D is essential for the absorption and utilization of calcium and phosphate and aids in the mobilization of bone calcium and maintenance of serum calcium concentrations.

In humans, cholecalciferol (vitamin D_3) is synthesized in the skin, from 7-dehydrocholesterol, on exposure to ultraviolet radiation, and obtained from the diet from fish liver oils and salt water fish. In the absence of adequate sunlight exposure, vitamin D_3 is an essential dietary nutrient. Vitamin D is metabolised by the liver to form 25-hydroxycholecalciferol (calcifediol), which is then converted in the kidneys to the active 1,25-dihydroxyvitamin D_3 (calcitriol). In its biologically active form, vitamin D_3 stimulates intestinal calcium absorption, incorporation of calcium into the osteoid, and release of calcium from bone tissue. In the small intestine, it promotes rapid and delayed calcium uptake. The passive and active transport of phosphate is also stimulated. In the kidney, it inhibits the excretion of calcium and phosphate by promoting tubular resorption. The production of parathyroid hormone (PTH) in the parathyroids is inhibited directly by the biologically active form of vitamin D_3. PTH secretion is inhibited further by the increased calcium uptake in the small intestine under the influence of biologically active vitamin D_3.

Pharmacokinetics

Vitamin D from nutritional sources and synthetic Vitamin D products are readily absorbed from the small intestine in the presence of dietary lipids and bile acids. Cholecalciferol is metabolised by the microsomal enzyme vitamin D-25-hydroxylase to form 25-hydroxycolecalciferol (25(OH)D3, calcidiol), the primary storage form of vitamin D_3. 25(OH)D3 undergoes a secondary hydroxylation within the kidney to form the predominant active metabolite 1,25-hydroxycolecalciferol (1,25(OH)2D3, calcitriol). The conversion to calcitriol is regulated by its own concentration, PTH, and serum concentrations of calcium and phosphate. The metabolites circulate in the blood bound to a specific α-globin. Vitamin D and its metabolites are excreted mainly in the bile and faeces.

Indications

[Pr]Sandoz D 10 000at 10,000 IU is indicated used in the treatment of hypophosphatemic vitamin D – resistant rickets and hypoparathyroidism.

Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Hypercalcemia and/or hypercalciuria,
- Nephrolithiasis (Renal calculi).
- Hypervitaminosis D
- Severe renal impairment
- Malabsorption syndrome,
- Abnormal sensitivity to the toxic effect of vitamin D

Precautions

Chronic or acute administration of excessive doses may lead to hypervitaminosis D, manifested by hypercalcemia and its sequelae.

The therapeutic index of Vitamin D products is narrow, and there is great interindividual variation in the dose that will lead to chronic toxicity. Daily doses of cholecalciferol ranging from 50 000 to 100 000 IU (1.25 to 2.5 mg) in adults and 1000 IU (25 mcg) in children may result in hypervitaminosis. Other Vitamin D products with shorter duration of action may have a lower propensity to accumulate and to cause hypercalcemia.

Early symptoms of hypercalcemia may include weakness, fatigue, somnolence, headache, anorexia, dry mouth, metallic taste, nausea, vomiting, vertigo, tinnitus, ataxia and hypotonia. Later and possibly more serious manifestations include nephrocalcinosis, renal dysfunction, osteoporosis in adults, and impaired growth in children, anemia, metastatic calcification, pancreatitis, generalized vascular calcification and seizures.

Periodic monitoring of serum calcium, phosphate, magnesium, and alkaline phosphatase is recommended for patients taking Vitamin D products. Serum calcium should be maintained in the range of 2.25-2.5 mmol/L and not allowed to exceed 2.75 mmol/L.

Drug interactions

Interacting Drug	Effect	Clinical Comment
Antacids (aluminum-containing)	Increased intestinal absorption of aluminum may lead to increased aluminum levels.	Avoid this combination if possible.

Antacids (magnesium-containing)	Hypermagnesemia may develop when these agents are used concurrently with vitamin D.	Monitor magnesium levels particularly in patients with chronic renal failure.
Anticonvulsants (e.g., phenytoin, phenobarbital, carbamazepine)	Strong CYP3A4 inducers can reduce vitamin D levels, potentially causing vitamin D deficiency.	Consider prophylactic vitamin D supplementation. Monitor serum 25(OH)D every 2 years; supplement with vitamin D if necessary
Cholestyramine, colestipol	Intestinal absorption of vitamin D may be impaired.	Patients should be advised to allow as much time as possible between the ingestion of these drugs and vitamin D.
Danazol	Danazol may increase the hypercalcemic response to vitamin D.	Monitor serum calcium levels.
Digoxin	Vitamin D or any analogues should be used with caution in patients taking digoxin. Hypercalcemia (which may result from concomitant use) may enhance the arrhythmogenic effects of digoxin.	Strict medical supervision is required. Monitor serum calcium levels.
Efavirenz	Increased metabolism of vitamin D via CYP24A induction leads to a deficiency state.	Consider prophylactic vitamin D supplementation.
Mineral oil	Intestinal absorption of vitamin D may be impaired.	Patients should be advised to allow as much time as possible between the ingestion of these drugs.
Orlistat	Intestinal absorption of vitamin D may be impaired.	Patients should be advised to allow as much time as possible between the ingestion of these drugs.
Sevelamer	Sevelamer may decrease the serum concentration of orally administered vitamin D.	Monitor serum 25(OH)D levels and adjust vitamin D or analogue dose if necessary.
Sucralfate	Increased intestinal absorption of aluminum from sucralfate may lead to increased aluminum levels.	Avoid this combination if possible.

Thiazide diuretics	Increased risk of hypercalcemia and associated calcium toxicity. Thiazides decrease renal excretion of calcium and increase calcium release from bone. Thiazides may also enhance the effect of parathyroid hormone and vitamin D on release of calcium from bone.	Monitor serum calcium levels with concomitant therapy.

Different Vitamin D products should not be administered concurrently.

Special Populations

Pregnancy: Studies have shown safe use of Vitamin D at doses up to 4000 IU (100 mcg) daily during pregnancy although studies in animals have shown reproductive toxicity. The recommended daily dose of Vitamin D in pregnant women in Canada is 600 IU (15 mcg) daily. Avoid the use of vitamin D in excess of the recommended dietary allowance during pregnancy unless potential benefits outweigh the possible adverse effects. Severe deficiency of vitamin D during pregnancy can result in maternal osteomalacia and lead to significant morbidity in both mother and fetus.

Hypercalcemia during pregnancy may also lead to suppression of parathyroid hormone release in the neonate, resulting in hypocalcemia, tetany and seizures.

Lactation: The recommended daily dose of Vitamin D in nursing women is 600 IU (15 mcg). Vitamin D and its metabolites are excreted in breast milk. However, Vitamin D may be deficient in maternal milk; therefore, breastfed infants may require supplementation. Use of excessive amounts of Vitamin D in nursing mothers may result in hypercalcemia in infants. A daily dose of 4,000 IU (100 mcg) should not be exceeded. When prescribing additional vitamin D to a breast-fed child the practitioner should consider the dose of any additional vitamin D given to the mother.

Monitoring and Laboratory Tests: The best indicator of vitamin D status is 25- hydroxyvitamin D or 25(OH)D serum concentration, as this level reflects total vitamin D exposure (from skin synthesis, food and supplements). However, there is no clinical benefit in monitoring vitamin D levels unless a clinical condition, such as malabsorption syndromes, chronic renal or liver failure, unexplained bone pain, unusual fractures, and other evidence of metabolic bone disorders, predisposes the patient to vitamin D deficiency. Other clinical situations where vitamin D testing is indicated include hypo- or hypercalcemia/hyperphosphatemia, hypo-or hyperparathyroidism, unexplained increases in serum alkaline phosphatase or patients with symptoms suggesting hypervitaminosis D. Testing for vitamin D levels may also be indicated when a patient is on medications that affect vitamin D metabolism or absorption (see Table 1).

Adverse effects

Vitamin D_3 (cholecalciferol) is generally well tolerated in doses that do not exceed the recommended daily intake. Chronic excessive dosing can lead to toxicity (see precautions).

Overdose

Symptoms: Acute intoxication with Vitamin D_3 (cholecalciferol) may cause hypervitaminosis D (See Precautions). Hypercalcemia is usually reversible, however, if metastatic calcification has occurred, severe renal or cardiac failure or even death may result (see PRECAUTIONS).

Treatment: Treatment of acute or chronic intoxication includes withdrawal of the Vitamin D_3 and any calcium supplements, maintenance of low-calcium diet, administration of oral IV fluids and, if needed, corticosteroids or calciuric diuretics, such as furosemide and ethacrymic acid, to decrease serum calcium concentrations. Peritoneal or hemodialysis with calcium free dialysate will help remove calcium.

If acute ingestion is recent, gastric lavage or emesis may minimize further absorption. If the drug has already passed through the stomach, administration of mineral oil may promote faecal elimination.

Hypercalcemia is usually reversible; however, if metastatic calcification has occurred, severe renal or cardiac failure or even death may result.

Dosage

At the higher doses of vitamin D used for active treatment, the range between therapeutic and toxic doses is narrow. The dosage of vitamin D_3 must be individualized with careful monitoring of serum calcium levels. Careful titration is necessary to avoid overdose. Dietary and other sources of vitamin D must be considered. Calcium intake should be adequate.

For Vitamin D resistant rickets: 12,000 to 500,000 IU (0.3-12.5 mg) daily.

For hypoparathyroidism: 50,000 to 200,000 IU (1.25-5 mg) daily. Calcium supplementation is also required.

Dosage Forms, Composition and Packaging

Each clear, red, oval, soft gelatin capsule, with "10" imprinted in white, contains 10,000 IU (0.25 mg) of Vitamin D_3 (Cholecalciferol).

Non-medicinal Ingredients (alphabetical order): FD&C Red No.40, FD&C Yellow No.6, Gelatin, Glycerin, Opacode S-1-7078 White, Purified Water, and Soybean Oil.

Available in HDPE bottles of 60's.

Do not use if safety seal is broken.
Keep out of reach and sight of children.

Storage

Store between 15-30°C. Protect from light

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

SANDOZ A Novartis Division

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