

Rite-D

Cholecalciferol 200,000 I.U.

Nutritional Supplement

DOSAGE & ADMINISTRATION

As directed by the physician. (It is recommended to have your serum Vitamin D₃ levels checked before using the supplementation).

Supplement Facts

Each soft gel capsule contains:

Vitamin-D₃ (Cholecalciferol) 200,000 I.U.

Note: 1 International Unit (IU) of Vitamin-D is equivalent to 0.025 mcg of Cholecalciferol.

DESCRIPTION

Rite-D capsules contain Cholecalciferol, a Vitamin D analogue also referred to as Vitamin D₃. It is a fat soluble vitamin and is a precursor of the active hormone 1, 25-dihydroxy cholecalciferol, also known as Calcitriol. Chemically it is (3 β , 5Z, 7E)-9, 10 secocholesta-5, 7, 10(19)-trien-3-ol and molecular formula is C₂₇H₄₄O.

CLINICAL PHARMACOLOGY

Mechanism of Action

Cholecalciferol is produced within the skin under the influence of UV radiation including sunlight. In its biologically active form, cholecalciferol 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 cholecalciferol. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active cholecalciferol.

Pharmacokinetics

Absorption

Cholecalciferol from nutritional sources is almost completely absorbed from within the gastro-intestinal tract in the presence of dietary lipids and bile acids.

Distribution & Metabolism

Cholecalciferol is stored in fat cells. Cholecalciferol is metabolized by microsomal hydroxylase to form 25-hydroxycholecalciferol (25(OH) D₃, Calcidiol), the primary storage form of vitamin D₃. 25(OH) D₃ undergoes a secondary hydroxylation within the kidney to form the predominant active metabolite 1, 25-hydroxycholecalciferol (1,25(OH)₂D₃, calcitriol). The metabolites circulate in the blood bound to a specific α -globin. After a single oral dose of cholecalciferol, the maximum serum concentrations of the primary storage form are reached after approximately 7 days.

Elimination

Cholecalciferol and its metabolites are excreted mainly in bile and faeces. 25(OH)D₃ is slowly eliminated with an apparent half-life in serum of about 50 days.

INDICATIONS

Rite-D (cholecalciferol) capsules are indicated in:

- Prevention of Vitamin D deficiency
- Treatment of Vitamin D deficiency
- Osteomalacia due to hepatobiliary disease
- Osteomalacia due to malabsorption
- Hypoparathyroidism
- Osteodystrophy

CONTRAINDICATIONS

Cholecalciferol must not be used in patients with:

- Hypersensitivity to the active substance (cholecalciferol or any Vitamin D analogue
- Hypercalcaemia and/or hypercalciuria
- Nephrolithiasis (Renal calculi)
- Hypervitaminosis D
- Severe renal impairment
- Metastatic calcification

WARNING AND PRECAUTIONS

Renal impairment

Cholecalciferol should be used with caution in patients with impairment of renal function due to the potential exacerbation related to hypercalcemic effects during therapeutic use. The effect on calcium and phosphate levels should also be monitored. The risk of soft tissue calcification should be taken into account. In patients with severe renal insufficiency, vitamin D in the form of cholecalciferol is not metabolized normally and other forms of vitamin D should be used.

Hepatic Impairment

In patients with liver impairment. Vitamin D absorption may be markedly impaired; conversion to active metabolite calcitriol may be reduced significantly, with the requirement of high doses of cholecalciferol. Agents not requiring hepatic hydroxylation are preferred in this condition. It is not reasonable to use cholecalciferol in severe liver impairment.

Renal calculi

Cholecalciferol should not be taken by patients with a tendency to form calcium containing renal calculi.

Cardiac disorders

Caution is required in patients receiving treatment for cardiovascular disease. There is a risk of potential exacerbation of cardiac disorders and arteriosclerosis related to persistent hypercalcemic effects during therapeutic use.

Sarcoidosis

Cholecalciferol should be prescribed with caution to patients suffering from sarcoidosis because of the risk of increased metabolism of vitamin to its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Serum calcium monitoring

All patients receiving high pharmacological doses of cholecalciferol and those with renal impairment should have their plasma calcium concentration monitored at intervals (initially once or twice weekly) and whenever nausea or vomiting occurs.

Calcium supplementation

Calcium supplementation should be considered for individual patients. Calcium supplements should be given under close medical supervision. Medical supervision is required whilst on treatment to prevent hypercalcaemia.

Risk of hypercalcaemia due to concomitant medications

Concurrent use of calcium containing preparations, other vitamin D-containing preparations or vitamin D analogs, or thiazide diuretics with cholecalciferol may predispose to (enhanced risk of hypercalcaemia). See DRUG INTERACTIONS

Hyperlipidemia

Cholecalciferol may cause a potential exacerbation of LDL elevation.

Hyperphosphatemia

There is a risk of metastatic calcification; normalization of phosphate levels is indicated prior to therapy with cholecalciferol.

Effects on ability to drive and use machines

Cholecalciferol has no known side effects that are likely to affect the ability to drive and use or operate machines.

ADVERSE REACTIONS

Vitamin D₃ (Cholecalciferol) is well-tolerated in therapeutic doses. Following adverse effects may occur however;

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia, Hypercalciuria

Skin and Subcutaneous disorders
Rare: Pruritus, Rash, Urticaria

Adverse effects observed with overdosage of Cholecalciferol (Hypervitaminosis - D) are given in OVERDOSAGE section.

DRUG INTERACTIONS

- Patients co-treated with cardiac glycosides along with cholecalciferol may be susceptible to high calcium levels and should have ECG parameters and calcium levels monitored. It is recommended to reduce the dose or interrupt treatment if the calcium content in the urine exceeds 7.5 mmol/24 hours (300 mg/24 hours).
- Simultaneous administration of benzothiadiazine derivatives (thiazide diuretics) increases the risk of hypercalcaemia because they decrease the calcium excretion in the urine. The calcium levels in plasma and urine should therefore be monitored for patients undergoing long-term treatment.
- If cholecalciferol is combined with metabolites or analogues of vitamin D careful monitoring of serum calcium levels is recommended.
- Anti-convulsants e.g. phenytoin, phenobarbital, primidone, carbamazepine may diminish the effect of cholecalciferol due to hepatic enzyme induction.
- Rifampicin may reduce the effectiveness of cholecalciferol due to hepatic enzyme induction.
- Isoniazid may reduce the effectiveness of cholecalciferol due to inhibition of the metabolic activation of cholecalciferol.
- Drugs leading to fat malabsorption. e.g. orlistat, liquid paraffin. cholestyramine, may impair the absorption of cholecalciferol.
- The cytotoxic agent actinomycin and imidazole antifungal agents interfere with vitamin 11 activity by inhibiting the conversion of 25-hydroxyvitamin D 1, 25-dihydroxyvitamin D by the kidney enzyme. 25-hydroxyvitamin D-1-hydroxylase.
- Concomitant use of glucocorticoids can decrease the effect of vitamin D.

USE IN SPECIAL POPULATIONS

Pregnancy

Therapeutic doses of cholecalciferol during pregnancy are unlikely to be harmful. However, Cholecalciferol should not be used during pregnancy unless the clinical condition of the woman requires treatment with cholecalciferol, at a dose necessary to overcome the deficiency.

Vitamin D overdose causes physical and mental disability and congenital heart and eye conditions, due to hypercalcaemia, when administered during pregnancy.

Nursing mothers

Cholecalciferol and its metabolites are excreted in breast milk. Caution is required with high doses to prevent the potential risk of hypercalcaemia in infants. Serum calcium monitoring is advised.

Pediatrics

Cholecalciferol capsules should not be given to infants and children under the age of 12 years.

Renal Impairment

No dosage adjustment is needed in patients with renal impairment. Cholecalciferol should be used with caution in patients with impairment of renal function due to the potential exacerbation related to hypercalcaemic effects during therapeutic use. Cholecalciferol must not be used in severe renal impairment metabolic as conversion to the active metabolite calcitriol is impaired and higher doses are generally required in most conditions. See WARNINGS AND PRECAUTIONS

Hepatic Impairment

No dosage adjustment is needed. For details see WARNINGS AND PRECAUTIONS

OVER DOSAGE Symptoms

Acute or chronic overdose of Cholecalciferol can cause hypercalcaemia, an increase in the serum and urinary concentrations of calcium. The symptoms of hypercalcaemia are not very specific and consist of nausea, vomiting, diarrhoea often in the early stages and later constipation, anorexia, fatigue, headache, muscle and joint pain, muscle weakness, polydipsia, polyuria formation of renal calculi, nephrocalcinosis, kidney failure and calcification of soft tissues, changes in ECG measurements, arrhythmias and pancreatitis. In rare and isolated cases there are reports that hypercalcaemia is fatal.

Treatment of overdose

A normalization of hypercalcaemia due to vitamin D intoxication lasts several weeks. The recommendation for the treatment of hypercalcaemia is the avoidance of any further administration of vitamin D, including supplements, dietary intakes and the avoidance of sunlight. A low calcium or calcium-free diet can also be considered.

Rehydration and the treatment with diuretics e.g. furosemide to ensure adequate diuresis should be considered. Additional treatment with calcitonin or corticosteroids can also be considered.

Phosphate infusions should not be administered to lower hypercalcaemia of hypervitaminosis D because of the dangers of metastatic calcification.

PRESENTATION

Rite-D (Cholecalciferol) 200,000IU: Pack of 1 Oral Soft Gel Capsule.

STORAGE

Store below 25°C.

Protect from sunlight & moisture.

The expiration date refers to the product correctly stored at the required conditions.

Manufactured by:

ICI PAKISTAN LTD.

Life Sciences Business,

5 West Wharf, Karachi-74000

Enlistment. No. 00152

ہدایات:

دوا کو ۲۵ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
دھوپ اور نمی سے بچائیں۔ بچوں کی پہنچ سے دور رکھیں۔

**SCILIFE**

Marketed by:

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