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SUPPLEMENT FACTS

Opt-D® Capsule 25,000 IU
Each oral soft gel capsule contains:
Cholecalciferol (Vitamin D_3) ..equivalent to 25,000 IU
Opt-D® Capsule 100,000 IU
Each oral soft gel capsule contains:
Cholecalciferol (Vitamin D_3)..equivalent to 100,000 IU
Opt-D® Capsule 200,000 IU
Each oral soft gel capsule contains:
Cholecalciferol (Vitamin D_3)..equivalent to 200,000 IU

1 International unit (IU) of vitamin D is equivalent to 0.025 mcg of Cholecalciferol

DESCRIPTION

Opt-D® capsules contain Cholecalciferol, a Vitamin D analogue also referred to as Vitamin D_3. 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 (3β, 5Z, 7E)-9, 10-secocholesta-5, 7, 10(19)-trien-3-ol and molecular formula is $C_{27}H_{44}O$.

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) D_3, calcidiol), the primary storage form of vitamin D_3. 25(OH) D_3 undergoes a secondary hydroxylation within the kidney to form the predominant active metabolite 1, 25-hydroxycholecalciferol (1, 25(OH)$2D_3$, 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) D_3 is slowly eliminated with an apparent half-life in serum of about 50 days.

INDICATIONS

Opt-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

DOSAGE AND ADMINISTRATION

Adult dosage:

Prevention of Vitamin-D deficiency:
25,000 IU capsule / month
Higher doses may be needed in certain population e.g. hospitalized individuals, dark skinned individuals, individuals with limited effective sun exposure, obese individuals, patients being evaluated for osteoporosis, patients using certain concomitant medications (e.g., anticonvulsant medications, glucocorticoids), patients with malabsorption, including inflammatory bowel disease and coeliac disease. In such populations monitoring of serum Vitamin D levels 25(OH)D is also recommended.

Treatment of Vitamin D deficiency:
50,000 IU (2 capsules of 25,000 IU) per week initially for 7 weeks. Followed by maintenance therapy with 2 capsules of 25,000 IU per month.

OR

1 capsule of 100,000 IU once every 3 months.
Follow-up 25(OH) D measurements should be made approximately three to four months after initiating maintenance therapy to confirm that the target level has been achieved)

Osteomalacia due to hepatobiliary disease:

50,000 IU (2 capsules of 25,000 IU) once daily

Osteomalacia due to malabsorption:

50,000 IU (2 capsules of 25,000 IU) once daily

Hypoparathyroidism:

For the treatment of hypocalcemia of hypoparathyroidism initially, vitamin D in oral doses of 50,000 to 200,000 units daily can be given as soon as acute tetany is controlled by intravenous calcium. Usual maintenance doses range from 25,000 to 100,000 units daily.

Osteodystrophy:

100,000 – 300,000 IU daily

Dosing in adolescent patients 12 - < 18 years of age:

Prevention of Vitamin-D deficiency:

1 capsule of 25,000 IU every 6 weeks

Treatment of Vitamin D deficiency:

1 capsule of 25,000 IU once every 2 weeks for duration of 6 weeks

Osteomalacia due to hepatobiliary disease:

10,000 IU – 25,000 IU daily

Osteomalacia due to malabsorption:

10,000 IU – 25,000 IU daily

Dosing considerations in special populations

Renal Impairment
No dosage adjustment required

Hepatic Impairment
No dosage adjustment required

Administration requirements
OPT-D® (Cholecalciferol) capsules should be taken orally and should be swallowed whole with water, preferably with the main meal of the day.

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 calcifediol 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 D 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 hypercalcemia 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 hypercalcemia). 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 cholecaciferol.

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 D_3 (Cholcalciferol) 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, carbamazapine 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 D activity by inhibiting the conversion of 25-hydroxyvitamin D to 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 hypercalcemia 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 hypercalcemic 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
Opt-D® (Cholecalciferol) 25,000IU : Pack of 4 Oral Soft Gel Capsules
Opt-D® (Cholecalciferol) 100,000IU : Pack of 2 Oral Soft Gel Capsules
Opt-D® (Cholecalciferol) 200,000IU : Pack of 1 Oral Soft Gel Capsule

INSTRUCTIONS
Dosage as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.

ہدایات:
ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
بچوں کی پہنچ سے دُور رکھیں۔
صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کی جائے۔
روشنی، گرمی اور نمی سے محفوظ، 30°C سے کم درجہ حرارت پر رکھیں۔

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