VIT D3 50000

Tablets

Composition

Each tablet contains Vitamin D_3 50000 IU (Cholecalciferol)

Action

Cholecalciferol is a vitamin D compound which possesses the property of preventing or treating rickets.
Vitamin D is essential for promoting absorption and utilization of calcium and phosphate and for normal calcification of bone. Along with parathyroid hormone and calcitonin, it regulates serum calcium concentrations by increasing serum calcium and phosphate concentrations as needed.

Vitamin D stimulates calcium and phosphate absorption from the small intestine and mobilizes calcium from bone.

Cholecalciferol is transferred to the liver where it is converted to calcifediol (25-hydroxycolecalciferol), which is then transferred to the kidneys and converted to calcitriol (1,25-dihyroxycolecalciferol, thought to be the most active form) and 24,25-dihydroxycolecalciferol (physiologic role not determined).

Calcitriol appears to act by binding to a specific receptor in the cytoplasm of the intestinal mucosa and subsequently being incorporated into the nucleus, probably leading to formation of the calcium-binding protein which results in increased absorption of calcium from the intestine. Also, calcitriol may regulate the transfer of calcium ion from bone and stimulate reabsorption of calcium in the distal renal tubule, thereby effecting calcium homeostasis in the extracellular fluid.

Onset of action – Hypercalcaemic: 12 to 24 hours; therapeutic effect may take 10 to 14 days.

Duration of action – Following oral administration: up to 6 months; repeated doses have a cumulative action.

Pharmacokinetics and Metabolism

Absorption

Vitamin D is well absorbed from the gastro-intestinal tract in the presence of bile, so the administration with the major meal of the day might therefore facilitate the absorption of Vitamin D.

Distribution and biotransformation

It is hydroxylated in the liver to form 25-hydroxy-colecalciferol and then undergoes further hydroxylation in the kidney to form the active metabolite 1, 25-dihydroxycolecalciferol (calcitriol).

Elimination

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.

Characteristics in Specific Groups of Subjects or Patients

A 57% lower metabolic clearance rate is reported in subjects with renal impairment as compared with that of healthy volunteers. Decreased absorption and increased elimination of vitamin D occurs in subjects with malabsorption. Obese subjects are less able to maintain vitamin D levels with sun exposure, and are likely to require larger oral doses of vitamin D to replace deficits.

Pharmacodynamics

In its biologically active form Vitamin D 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 for m of vitamin D_3. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active e vitamin D.

Indications
The treatment of vitamin D deficiency.

Contraindications
• Hypersensitivity to the active substance.
• Hypercalcaemia and/or hypercalciuria.
• Nephrolithiasis and/or nephrocalcinosis
• Serious renal impairment
• Hypervitaminosis D
• Pseudohypoparathyroidism as the vitamin D requirement may be reduced due to phases of normal vitamin D sensitivity, involving the risk of prolonged overdose. Better-regulatable vitamin D derivatives are available for this.

Warnings & Precautions
Vitamin D should be used with caution in patients with impairment of renal function and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account.

Caution is required in patients receiving treatment for cardiovascular disease .

VitD3 should be prescribed with caution in patients with sarcoidosis, due to a possible increase in the metabolism of vitamin D in its active form. In these patients the serum and urinary calcium levels should be monitored.

Allowances should be made for the total dose of vitamin D in cases associated with treatments already containing vitamin D, foods enriched with vitamin D, cases using milk enriched with vitamin D, and the patient's level of sun exposure.

There is no clear evidence for causation between vitamin D supplementation and renal stones, but the risk is plausible, especially in the context of concomitant calcium supplementation. The need for additional calcium supplementation should be considered for individual patients. Calcium supplements should be given under close medical supervision.

Oral administration of high-dose vitamin D (500,000 IU by single annual bolus) was reported to result in an increased risk of fractures in elderly subjects, with the greatest increase occurring during the first 3 months after dosing.

Pregnancy
Category C
There are no or limited amount of data from the use of Cholecalciferol in pregnant women. Studies in animals have shown reproductive toxicity . The recommended daily intake for pregnant women is 400 IU, however, in women who are considered to be vitamin D deficient a higher dose may be required (up to 2000 IU/day).

During pregnancy women should follow the advice of their medical practitioner as their requirements may vary depending on the severity of their disease and their response to treatment vitamin D and its metabolites are excreted in breast milk.

Nursing Mothers
Vitamin D can be prescribed while the patient is breast-feeding if necessary. This supplementation does not replace the administration of vitamin D in the neonate.

Geriatric Use

Studies have shown that the elderly may have an increased need for vitamin D due to a possible decrease in the capacity of the skin to produce pre-vitamin D, or a decrease in exposure to the sun or impaired renal function or impaired vitamin D absorption.

Adverse Reactions

Note:
Ingestion of excessive doses of vitamin D either as an acute overdose or over prolonged periods can result in severe toxicity.

Chronic vitamin D-induced hypercalcaemia may result in generalized vascular calcification, nephrocalcinosis, and other soft tissue calcification that may lead to hypertension and renal failure. These effects are more likely to occur when the hypercalcaemia is accompanied by hyperphosphatamia.

Growth may be arrested in children, especially after prolonged administration of 45mcg (1800 units) of Cholecalciferol per day.

Death may occur as a result of renal or cardiovascular failure caused by vitamin D toxicity.

Dosage necessary to cause toxicity varies with individual sensitivity, but in individuals without malabsorption problems, 250mcg (10,000 units) a day for more than several weeks or months is the maximum dose.

Toxicity may occur with therapeutic doses of calcitriol.

The following side / adverse effects have been selected on the basis of their potential clinical significance (possible signs and symptoms in parentheses where appropriate) – not necessarily inclusive.

Those indicating need for medical attention
Early symptoms of vitamin D toxicity associated with hypercalcaemia
Constipation – usually more frequent in children and adolescents; diarrhea; dryness of mouth; headache, continuing; increased thirst; increase in frequency of urination, especially at night, or in amount of urine; loss of appetite; metallic taste; nausea or vomiting –usually more frequent in children and adolescents; unusual tiredness or weakness.

Late symptoms of vitamin D toxicity associated with hypercalcaemia
Bone pain; cloudy urine; high blood pressure; increased sensitivity of eyes to light or irritation of eyes; irregular heartbeat; itching of skin; lethargy (drowsiness); muscle pain; nausea or vomiting and pancreatitis (stomach pain, severe); psychosis, overt (mood or mental changes); -rare; weight loss.

The following reactions have been reported as causally related to vitamin D intake:
face oedema, genital oedema, pruritus, dry skin, nail disorder, erythematosus rash, decreased prothrombin (drug interaction), purpuric rash, choking, and dysphagia.
The decreased prothrombin was assessed as severe and as arising due to a possible interaction of Vitamin D with warfarin and calcium carbonate.

Concomitant use of anticonvulsants (such as phenytoin) or barbiturates (and possibly other drugs that induce hepatic enzymes) may reduce the effect of vitamin D3 by metabolic inactivation.

In cases of treatment with thiazide diuretics, which decrease urinary elimination of calcium, monitoring of serum calcium concentration is recommended.

Drug Interactions

Concomitant use of anticonvulsants (such as phenytoin) or barbiturates (and possibly other drugs that induce hepatic enzymes) may reduce the effect of vitamin D3 by metabolic inactivation.

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Concomitant use of glucocorticoids can decrease the effect of vitamin D.

In cases of treatment with drugs containing digitalis and other cardiac glycosides, the administration of vitamin D may increases the risk of digitalis toxicity (arrhythmia). Strict medical supervision is needed, together with serum calcium concentration and electrocardiographic monitoring if necessary.

Simultaneous treatment with ion exchange resin such as cholestyramine, colestipol hydrochloride, orlistat or laxative such as paraffin oil may reduce the gastrointestinal absorption of vitamin D.

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.

Dosage and Administration

Treatment of vitamin D deficiency (<25 nmol/l) 50,000 IU/week (1single-dose) for 6-8 weeks, followed by maintenance therapy (equivalent to 1400-2000 IU/day, such as 1 single-dose 50,000 IU oral / month) may be required; 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).

Certain populations are at high risk of vitamin D deficiency, and may require higher doses and monitoring of serum 25(OH)D:
- Institutionalized or hospitalized individuals
- Dark skinned individuals
- Individuals with limited effective sun exposure due to protective clothing or consistent use of sun screens
- Obese individuals
- Patients being evaluated for osteoporosis
- Use of certain concomitant medications (e.g., anticonvulsant medications, glucocorticoids)
- Patients with malabsorption, including inflammatory bowel disease and coeliac disease
- Those recently treated for vitamin D deficiency, and requiring maintenance therapy.

Special populations
Renal impairment
invitaD3 should not be used in combination with calcium in patients with severe renal impairment.

Hepatic impairment
No posology adjustment is required in patients with hepatic impairment.

Method of administration
Patients should be advised to take VIT D3 50000 IU preferably with meal.

Administration to adults:
The single-dose should be either emptied into the mouth and swallowed orally, or emptied onto a spoon and taken orally. VIT D3 50000 IU can also be taken by mixing with a small amount of cold or lukewarm food/drink immediately prior to use.

Over Dosage

Symptoms of overdose
Ergocalciferol (vitamin D2) and Cholecalciferol (vitamin D3) have a relatively low therapeutic index. The threshold for vitamin D intoxication is between 40,000 and 100,000 IU daily for 1 to 2 months in adults with normal parathyroid function. Infants and small children may react sensitively to far lower concentrations. Therefore, it is warned against intake of vitamin D without medical supervision.

Overdose leads to increased serum and urinary phosphorus levels, as well as hypercalcaemic syndrome and consequently calcium deposits in the tissues and above all in the kidneys (nephrolithiasis, nephrocalcinosis) and the vessels.

Discontinue Vit.D3 when calcaemia exceeds 10.6 mg/dl (2.65 mmol/l) or if the calciuria exceeds 300 mg/24 hours in adults or 4-6 mg/kg/day in children.

Chronic overdosage may lead to vascular and organ calcification, as a result of hypercalcaemia.

The symptoms of intoxication are little characteristic and manifest as nausea, vomiting, initially also diarrhoea, later constipation, loss of appetite, weariness, headache, muscle pain, joint pain, muscle weakness, persistent sleepiness, azotaemia, polydipsia and polyuria and, in the final stage, dehydration. Typical biochemical findings include hypercalcaemia, hypercalciuria, as well as increased serum 25 hydroxy colecalciferol concentrations.

Treatment of over dose
Symptoms of chronic vitamin D overdosage may require forced diuresis as well as administration of glucocorticoids or calcitonin.

Overdosage requires measures for treating the - often persisting and under certain circumstances life-threatening - hypercalcaemia.

The first measure is to discontinue the vitamin D preparation; it takes several weeks to normalize hypercalcaemia caused by vitamin D intoxication.

Depending on the degree of hypercalcaemia, measures include a diet that is low in calcium or free of calcium, abundant liquid intake, increase of urinary excretion by means of the drug furosemide, as well as the administration of glucocorticoids and calcitonin.

If kidney function is adequate, calcium levels can be reliably lowered by infusions of isotonic sodium chloride solution (3–6 liters in 24 hours) with addition of furosemide and, in some circumstances, also 15 mg/kg body weight/hour sodium edetate accompanied by continuous calcium and ECG monitoring. In oligoanuria, in contrast, haemodialysis (calcium-free dialysate) is necessary.

No special antidote exists.

It is recommended to point out the symptoms of potential overdose to patients under chronic therapy with higher doses of vitamin D (nausea, vomiting, initially also diarrhoea, later constipation, anorexia, weariness, headache, muscle pain, joint pain, muscle weakness, persistent sleepiness, azotaemia, polydipsia and polyuria).

Presentation
Jar of 6 Tablets