VITAMIN D3 (CHOLECALCIFEROL)

Cholecalciferol (vitamin D3) is a steroid hormone that has long been known for its important role in regulating body levels of calcium and phosphorus, in mineralization of bone, and for the assimilation of Vitamin A. The classical manifestations of vitamin D deficiency is rickets, which is seen in children and results in bony deformaties including bowed long bones. Deficiency in adults leads to the disease osteomalacia. Both rickets and osteomalacia reflect impaired mineralization of newly synthesized bone matrix, and usually result from a combination of inadequate exposure to sunlight and decreased dietary intake of vitamin D. Common causes of vitamin D deficiency include genetic defects in the vitamin D receptor, severe liver or kidney disease, and insufficient exposure to sunlight. Vitamin D plays an important role in maintaining calcium balance and in the regulation of parathyroid hormone (PTH). It promotes renal reabsorption of calcium, increases intestinal absorption of calcium and phosphorus, and increases calcium and phosphorus mobilization from bone to plasma.

Cholecalciferol for patients

The patient and his or her parents or s.o.s. should be informed about compliance with dosage instructions, adherence to instructions about diet and calcium supplementation and avoidance of the use of unapproved nonprescription drugs. Patients should also be carefully informed about the symptoms of hypercalcemia.

The effectiveness of vitamin D therapy is predicated on the assumption that each patient is receiving an adequate daily intake of calcium. Patients are advised to have a dietary intake of calcium at a minimum of 600 mg daily. The U.S. RDA for calcium in adults is 800 mg to 1200 mg.

Cholecalciferol Interactions

Interactions for vitamin D analogues (Vitamin D2, Vitamin D3, Calcitriol, and Calcidiol):

Cholestyramine:

Cholestyramine has been reported to reduce intestinal absorption of fat soluble vitamins; as such it may impair intestinal absorption of any of vitamin D.

Phenytoin/Phenobarbital:

The coadministration of phenytoin or phenobarbital will not affect plasma concentrations of vitamin D, but may reduce endogenous plasma levels of calcitriol/ergocalcitriol by accelerating metabolism. Since blood level of calcitriol/ergocalcitriol will be reduced, higher doses of Rocaltrol may be

necessary if these drugs are administered simultaneously.

Thiazides:

Thiazides are known to induce hypercalcemia by the reduction of calcium excretion in urine. Some reports have shown that the concomitant administration of thiazides with vitamin D causes hypercalcemia. Therefore, precaution should be taken when coadministration is necessary.

Digitalis:

Vitamin D dosage must be determined with care in patients undergoing treatment with digitalis, as hypercalcemia in such patients may precipitate cardiac arrhythmias.

Ketoconazole:

Ketoconazole may inhibit both synthetic and catabolic enzymes of vitamin D. Reductions in serum endogenous vitamin D concentrations have been observed following the administration of 300 mg/day to 1200 mg/day ketoconazole for a week to healthy men. However, in vivo drug interaction studies of ketoconazole with vitamin D have not been investigated.

Corticosteroids:

A relationship of functional antagonism exists between vitamin D analogues, which promote calcium absorption, and corticosteroids, which inhibit calcium absorption.

Phosphate-Binding Agents:

Since vitamin D also has an effect on phosphate transport in the intestine, kidneys and bones, the dosage of phosphate-binding agents must be adjusted in accordance with the serum phosphate concentration.

Vitamin D:

The coadministration of any of the vitamin D analogues should be avoided as this could create possible additive effects and hypercalcemia.

Calcium Supplements:

Uncontrolled intake of additional calcium-containing preparations should be avoided.

Magnesium:

Magnesium-containing preparations (eg, antacids) may cause hypermagnesemia and should therefore not be taken during therapy with vitamin D by patients on chronic renal dialysis.

Cholecalciferol Contraindications

Contraindications for vitamin D analogues (Vitamin D2, Vitamin D3, Calcitriol, and Calcidiol):

Vitamin D should not be given to patients with hypercalcemia or evidence of vitamin D toxicity.

Use of vitamin D in patients with known hypersensitivity to vitamin D (or drugs of the same class) or any of the inactive ingredients is contraindicated.

Additional information about Cholecalciferol

Cholecalciferol Indication: For the treatment of vitamin D deficiency or insufficiency, refractory rickets (vitamin D resistant rickets), familial hypophosphatemia and hypoparathyroidism, and in the management of hypocalcemia and renal osteodystrophy in patients with chronic renal failure undergoing dialysis. Also used in conjunction with calcium in the management and prevention of primary or corticosteroid-induced osteoporosis.

Mechanism Of Action: The first step involved in the activation of vitamin D3 is a 25-hydroxylation which is catalysed by the 25-hydroxylase in the liver and then by other enzymes. The mitochondrial sterol 27-hydroxylase catalyses the first reaction in the oxidation of the side chain of sterol intermediates. The active form of vitamin D3 (calcitriol) binds to intracellular receptors that then function as transcription factors to modulate gene expression. Like the receptors for other steroid hormones and thyroid hormones, the vitamin D receptor has hormone-binding and DNA-binding domains. The vitamin D receptor forms a complex with another intracellular receptor, the retinoid-X receptor, and that heterodimer is what binds to DNA. In most cases studied, the effect is to activate transcription, but situations are also known in which vitamin D suppresses transcription. Calcitriol increases the serum calcium concentrations by: increasing GI absorption of phosphorus and calcium, increasing osteoclastic resorption, and increasing distal renal tubular reabsorption of calcium. Calcitriol appears to promote intestinal absorption of calcium through binding to the vitamin D receptor in the mucosal cytoplasm of the intestine. Subsequently, calcium is absorbed through formation of a calcium-binding protein.

Drug Interactions: Not Available

Food Interactions: Not Available

Generic Name: Cholecalciferol

Synonyms: Vitamin D3; CC; Cholecalciferol, D3; Colecalciferol

Drug Category: Antihypocalcemic Agents; Antihypoparathyroid Agents; Essential Vitamin; Vitamins (Vitamin D)