For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

CALFLASH 1000
CALFLASH 2000

(Calcium with Vitamin D_3 Tablets)

COMPOSITION

CALFLASH 1000

Each film coated tablet contains :

Calcium Carbonate I.P.	1.25 gm
equivalent toElemental Calcium	500 mg
Vitamin D_3 I.P.	1000 IU
Excipients	q.s.

(Appropriate overages added)
Colours : Brilliant Blue FCF, Tartrazine FCF

CALFLASH 2000

Each film coated tablet contains :

Calcium Carbonate I.P.	1.25 gm
equivalent to Elemental Calcium	500 mg
Vitamin D_3 I.P.	2000 IU
Excipients	q.s.

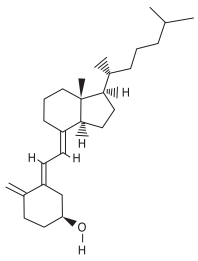
(Appropriate overages added)
Colours : Titanium Dioxide I.P.

DESCRIPTION

Vitamin D_3 *(Cholecalciferol)*

Cholecalciferol is the naturally occurring form of Vitamin D_3. It is produced from 7-dehydrocholesterol, a sterol present in mammalian skin, by ultraviolet irradiation. It's empirical formula is $C_{27}H_{44}O$, and molecular weight is 384.6.

It is chemically as (5Z,7E)-(3S)-9,10-secocholesta-5,7,10(19)-triene-3-ol.



Calcium

Calcium is a mineral that is present naturally in the food. It is necessary for many normal functions of body mainly, bone formation and maintenance.

CLINICAL PHARMACOLOGY

Vitamin D_3 increases the intestinal absorption of calcium. Administration of calcium and Vitamin D_3 counteracts the increase of parathyroid hormone (PTH) which is caused by calcium deficiency and which causes increased bone resorption.

Pharmacokinetic

Calcium

Absorption: The amount of calcium absorbed through the gastrointestinal tract is approximately 30% of the swallowed dose.

Distribution and metabolism: 99% of the calcium in the body is concentrated in the hard structure of bones and teeth. The remaining 1% is present in the intra - and extracellular fluids. About 50% of the total blood-calcium content is in the physiologically active ionised form with approximately 10% being complexed to citrate, phosphate or other anions, the remaining 40% being bound to proteins, principally albumin.

Elimination: Calcium is eliminated through faeces, urine and sweat. Renal excretion depends on glomerular filtration and calcium tubular reabsorption.

Vitamin D_3

Absorption: Vitamin D_3 is easily absorbed in the small intestine.

Distribution and metabolism: Vitamin D_3 and its metabolites circulate in the blood bound to a specific globulin. Vitamin D_3 is converted in the liver by hydroxylation to the active form 25-hydroxycholecalciferol.

It is then further converted in the kidneys to 1,25 hydroxycholecalciferol; 1,25 hydroxy-cholecalciferol is the metabolite responsible for increasing calcium absorption.

Vitamin D_3 which is not metabolised is stored in adipose and muscle tissues.

Elimination: Vitamin D_3 is excreted in faeces and urine.

INDICATIONS

To be used during calcium deficiency, supplementation of calcium during growth, pregnancy, lactation or as directed by the Physician. It may be used as an adjunct to specific therapy for osteoporosis or as a therapeutic supplement in established osteomalacia, pregnant patients at high risk of needing such a therapeutic supplementation or malnutrition when dietary intake is less than that required.

CONTRAINDICATION

- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria
- Nephrolithiasis
- Hypervitaminosis D
- Hypersensitivity to the active substances or to any of the excipients

WARNINGS AND PRECAUTIONS

During long-term treatment, serum calcium levels should be followed and renal function should be monitored through measurement of serum creatinine. Monitoring is especially important in elderly patients on concomitant treatment with cardiac glycosides or diuretics and in patients with a high tendency to calculus formation. In case of hypercalcaemia or signs of impaired renal function, the dose should be reduced or the treatment discontinued.

Vitamin D_3 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. In patients with severe renal insufficiency, Vitamin D_3 in the form of Cholecalciferol is not metabolised normally and other forms of Vitamin D_3 should be used.

Should be prescribed with caution to patients suffering from sarcoidosis because of the risk of increased metabolism of Vitamin D_3 to its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Used with caution in immobilised patients with osteoporosis due to the increased risk of hypercalcaemia.

Caution should be exercised while prescribing Cholecalciferol and other medicinal products containing Vitamin D_3 or nutrients (such as milk). Additional doses of calcium or Vitamin D_3 increase the risk of hypercalcaemia with subsequent kidney function impairment and milk-alkali syndrome; therefore they should be taken under close medical supervision. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.

DRUG INTERACTION

Thiazide diuretics reduce the urinary excretion of calcium. Due to increased risk of hyper-calcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics.

Systemic corticosteroids reduce calcium absorption. During concomitant use, it may be necessary to increase the dose of dosage form.

Simultaneous treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce the gastrointestinal absorption of Vitamin D_3.

Calcium carbonate may interfere with the absorption of concomitantly administered tetracycline preparations. For this reason, tetracycline preparations should be administered at least two hours before, or four to six hours after, oral intake of calcium.

Hypercalcaemia may increase the toxicity of cardiac glycosides during treatment with calcium and Vitamin D_3. Patients should be monitored with regard to electrocardiogram (ECG) and serum calcium levels.

If a bisphosphonate or sodium fluoride is used concomitantly, this preparation should be administered at least three hours before the intake of tablet(s) since gastrointestinal absorption may be reduced.

The efficacy of levothyroxine can be reduced by the concurrent use of calcium, due to decreased levothyroxine absorption. Administration of calcium and levothyroxine should be separated by at least four hours.

The absorption of quinolone antibiotics may be impaired if administered concomitantly with calcium. Quinolone antibiotics should be taken two hours before or after intake of calcium.

Oxalic acid (found in spinach and rhubarb) and phytic acid (found in whole cereals) may inhibit calcium absorption through formation of insoluble calcium salts. The patient should not take calcium products within two hours of eating foods high in oxalic acid and phytic acid.

ADVERSE EVENTS

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: uncommon (1/1,000, to < 1/100); rare (1/10,000 to < 1/1,000) or very rare (1/10,000)

Metabolism and nutrition disorders

Uncommon: Hypercalcaemia and hypercalciuria.

Very rare: Seen usually only in overdose : Milk-alkali syndrome

Gastrointestinal disorders

Rare: Constipation, dyspepsia, flatulence, nausea, abdominal pain and diarrhoea.

Skin and subcutaneous disorders

Rare: Pruritus, rash and urticaria.

Overdose

Overdose can lead to hypervitaminosis D and hypercalcaemia. Symptoms of hyper-calcaemia may include anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, mental disturbances, polydipsia, polyuria, bone pain, nephrocalcinosis, nephrolithiasis and in severe cases, cardiac arrhythmias. Extreme hypercalcaemia may result in coma and death. Persistently high calcium levels may lead to irreversible renal damage and soft tissue calcification.

Milk-alkali syndrome (frequent urge to urinate; continuing headache; continuing loss of appetite; nausea or vomiting; unusual tiredness or weakness; hypercalcaemia, alkalosis and renal impairment). The milk-alkali syndrome of hypercalcaemia, alkalosis and renal impairment still occur in patients who ingest large amounts of calcium and absorbable alkali; it is not uncommon as a cause of hypercalcaemia requiring hospitalisation. The syndrome has also been reported in a patient taking recommended doses of antacids containing calcium carbonate for chronic epigastric discomfort, and in a pregnant woman taking high, but not grossly excessive, doses of calcium (about 3 g of elemental calcium daily). Metastatic calcification can develop.

Treatment of hypercalcaemia

The treatment with Calcium and Vitamin D_3 must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A and cardiac glycosides must also be discontinued. Treatment is rehydration, and, according to severity of hypercalcaemia, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids should be considered. Serum electrolytes, renal function and diuresis must be monitored. In severe cases, ECG and CVP should be followed.

DOSAGES AND ADMINISTRATION

Oral

Adjunctive therapy in osteoporosis

One tablet 2-3 times per day

Calcium and Vitamin D_3 deficiency

Adults

One tablet 2-3 times per day

Children

One tablet 1-2 times per day

Dosage in hepatic impairment

No dose adjustment is required.

Dosage in renal impairment

Should not be used in patients with severe renal impairment.

Pregnancy

During pregnancy the daily intake should not exceed 1500 mg calcium and 600 IU Vitamin D_3. Studies in animals have shown reproductive toxicity with high doses of Vitamin D_3. In pregnant women, overdoses of calcium and Vitamin D_3 should be avoided as permanent hypercalcaemia has been related to adverse effects on the developing foetus. There are no indications that Vitamin D_3 at therapeutic doses is teratogenic in humans. Calcium and Vitamin D_3 tablets can be used during pregnancy, in case of a calcium and Vitamin D_3 deficiency.

Lactation

Calcium and Vitamin D_3 tablets can be used during breast-feeding. Calcium and Vitamin D_3 pass into breast milk. This should be considered when giving additional Vitamin D_3 to the child.

EXPIRY DATE

Do not use later than the date of expiry.

STORAGE

Store below 25^{o}C in a dry place. Protect from direct sunlight.

Keep all medicines out of reach of children.

PRESENTATION

CALFLASH 1000 and CALFLASH 2000 are available as blister strip of 10 tablets.

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Marketed by :
TORRENT PHARMACEUTICALS LTD.
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