1. Name of the Medicinal Product

CAL D3 (Calcium and Colecalciferol Tablets BP)

2. Qualitative and Quantitative Composition

Composition:

Each film coated tablet contains:

Calcium Carbonate	BP	1250mg
Eq. to Elemental Calcium		500mg
Colecalciferol (Vitamin D3)	BP	250mg
Excipients		q.s.

Approved colour used

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

Solid Oral Dosage Form (Tablets)

4. Clinical Particulars

4.1 Therapeutic Indications

The treatment and prevention of vitamin D/calcium deficiency (characterised by raised serum alkaline phosphatase levels associated with increased bone loss, raised levels of serum PTH and lowered 25-hydroxyvitamin D) particularly in the housebound and institutionalized elderly subjects.

The supplementation of vitamin D and calcium as an adjunct to specific therapy for osteoporosis, in pregnancy, in established vitamin D dependent osteomalacia, and in other situations requiring therapeutic supplementation of malnutrition.

4.2 Posology and Method of Administration

Posology

Adults and elderly:

Adjunctive therapy in osteoporosis and Calcium and vitamin D deficiency.

One tablet twice daily

Special Patient Populations

Paediatric population

Cal D3 Tablets are not intended for use in children.

Impaired hepatic function

No dose adjustment is required.

Impaired renal function

Cal D3 Tablets should not be used in patients with severe renal impairment.

Method of Administration

Oral

4.3 Contraindications

• Hypersensitivity to the active substances or to any of the excipients

• Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria

• Severe renal impairment (glomerular filtration rate < 30 ml/min)

• Renal calculi (nephrolithiasis)

• Hypervitaminosis D

4.4 Special Warning and Precautions for Use

During long-term treatment, serum calcium levels should be followed and renal function should be monitored through measurements of serum creatinine. Monitoring is especially important in 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.

Cal D3 Tablets should be used with caution in patients with hypercalcaemia or signs of impaired 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 in the form of colecalciferol is not metabolized normally and other forms of vitamin D should be used.

During concomitant treatment with other high dose sources of vitamin D and/or medications or nutrients (such as milk) containing calcium, there is a risk of hypercalcaemia and milk-alkali syndrome with subsequent kidney function impairment.

In these patients serum calcium levels should be followed and renal function should be monitored.

Cal D3 Tablets should be prescribed with caution to patients suffering from sarcoidosis because of the risk of increased metabolism of vitamin D3 to its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Cal D3 Tablets should be used with caution in immobilised patients with osteoporosis due to the increased risk of hypercalcaemia.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

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

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 carbonate.

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

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 six hours after intake of calcium.

If a bisphosphonate is used concomitantly, this preparation should be administered at least one hour before the intake of Cal D3 Tablets since gastrointestinal absorption may be reduced.

Calcium salts may decrease the absorption of iron, zinc and strontium ranelate. Consequently, iron, zinc or strontium ranelate preparations should be taken at least two hours before or after Cal D3 Tablets.

Treatment with orlistat may potentially impair the absorption of fat-soluble vitamins.

4.6 Fertility, pregnancy and lactation

Pregnancy

CAL D3 Tablets can be used during pregnancy, in case of a calcium and vitamin D deficiency. During pregnancy the daily intake should not exceed 2500 mg calcium and 4000 IU vitamin D. Studies in animals have shown reproductive toxicity with high doses of vitamin D. In pregnant women, overdoses of calcium and vitamin D should be avoided as permanent hypercalcaemia has been related to adverse effects on the developing foetus. There are no indications that vitamin D at therapeutic doses is teratogenic in humans.

Lactation

Cal D3 Tablets can be used during breast-feeding. Calcium and vitamin D3 pass into breast milk. This should be considered when giving additional vitamin D to the child.

4.7 Effects on Ability to Drive and Use Machines

Cal D3 Tablets have no known influence on the ability to drive and use machines.

4.8 Undesirable Effects

Immune system disorders

Not known: Hypersensitivity reactions such as angio-oedema or laryngeal oedema.

Metabolism and nutrition disorders

Uncommon: Hypercalcaemia and hypercalciuria.

Very rare: 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).

Gastrointestinal disorders

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

Skin and subcutaneous disorders

Rare: Pruritus, rash and urticaria.

4.9 Overdose

Symptoms

Overdose can lead to hypercalcaemia and hypervitaminosis D. Symptoms of hypercalcaemia 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 may occur in patients who ingest large amounts of calcium and absorbable alkali.

Treatment of hypercalcaemia

Treatment is essentially symptomatic and supportive. The treatment with calcium must be discontinued. Treatment with thiazide diuretics and cardiac glycosides must also be discontinued.

Treatment: 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.

5.0 Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Mineral supplements, Calcium, combinations with vitamin D and/or other drugs.

ATC code: A12AX

Vitamin D3 increases the intestinal absorption of calcium.

Administration of calcium and vitamin D3 counteracts the increase of parathyroid hormone (PTH), which is caused by calcium deficiency and which causes increased bone resorption.

5.2 Pharmacokinetic properties

Calcium

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

Distribution and biotransformation: 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.

Colecalciferol

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

Distribution and biotransformation: Colecalciferol and its metabolites circulate in the blood bound to a specific globulin.

Colecalciferol is converted in the liver by hydroxylation to 25-hydroxycholecalciferol. It is then further converted in the kidneys to the active form 1,25-dihydroxycholecalciferol; 1,25-dihydroxycholecalciferol is the metabolite responsible for increasing calcium absorption. Vitamin D3, which is not metabolised, is stored in adipose and muscle tissues.

Elimination: Vitamin D3 is excreted in faeces and urine.

5.3 Preclinical Safety Data

At doses far higher than the human therapeutic range teratogenicity has been observed in animal studies.

6. Pharmaceutical Particulars

6.1 List of Excipients

- Maize Starch BP
- Methyl Hydroxybenzoate BP
- Propyl Hydroxybenzoate BP
- Gelatin BP
- Dibasic Calcium Phosphate BP
- Lactose BP
- Purified Talc BP
- Hydrogenated Castor Oil BP
- Magnesium Stearate BP
- Sodium Starch Glycolate BP
- Croscarmellose Sodium BP
- Colloidal Anhydrous Silica BP
- Sheffcoat PVA White (5Y00328) IH
- Colour Ponceau 4R Supra IH
- Colour Ponceau 4R Lake IH
- Purified Water BP

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Store in a cool dry & dark place at a temperature not exceeding 25°C.

Keep the medicine out of reach of children.

6.5 Nature and Contents of Container

15 Tablets packed in ALU-PVC blister and such 2 blisters are packed in a unit carton along with pack insert.

6.6 Special Precautions for Disposal and Other Handling

Not applicable.

7. Registrant/Sole Agent

Embassy Pharmaceutical & Chemical Ltd.

41, Ademola Street, South West Ikoyi, Lagos, Nigeria. Tel: 01-2900791

8. Manufacturer

LABORATE PHARMACEUTICALS INDIA LIMITED

Unit-II, 31, Rajban Road, Nariwala, Paonta Sahib,

District Sirmour, Himachal Pradesh (India).

H.O.: E-11, Industrial Area, Panipat-132103

9. Date of Revision of Text

To be given after approval of product.

10. Dosimetry (If applicable)

Not applicable

11. Instructions for Preparation of Radiopharmaceuticals (If applicable)

Not applicable