1. Name of the Medicinal Product

1.1 Name of the Medicinal Product

CAL D3 PLUS

Calcium Carbonate, Vitamin D3, Magnesium Oxide and Zinc Sulphate Tablets

1.2. Strength

Calcium Carbonate	500 mg
Vitamin D3	200 IU
Magnesium Oxide	100 mg
Zinc Sulphate Monohydrate	7.5 mg
Excipients	q.s.

Approved colour used.

1.3. Pharmaceutical Dosage Form

Solid dosage form (Tablet)

Qualitative and Quantitative Composition

Qualitative Declaration

The **CAL D3 PLUS** Contains Calcium Carbonate, Vitamin D3, Magnesium Oxide and Zinc Sulphate.

Quantitative Declaration

Each film coated tablet contains:

Calcium Carbonate	BP	500 mg
Vitamin D3	BP	200 IU
Magnesium Oxide	BP	100 mg
Zinc Sulphate Monohydrate	BP	7.5 mg
Excipients		q.s.

Approved colour used.

3. Pharmaceutical Form

Solid dosage form (Tablet)

4. Clinical Particulars

4.1 Therapeutic Indications

Cal D3 Plus Tablets is indicated for the following conditions:-

- As a nutritional supplement for teen, young adult and post menopausal women.
- Helps build strong bones and teeth.
- May reduce the risk of osteoporosis.
- Helps support healthy muscle contraction.

4.2 Posology and Method of Administration

Oral

Adults and Elderly and children above 12 years of age: 2 tablets per day, preferably one tablet each morning and evening.

Children:

Not recommended for children under 12 years.

Or as directed by the physician.

Method of administration

For Oral Use Only.

4.3 Contraindications

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

• Severe renal impairment (glomerular filtration rate < 30 ml/min/1.73m2)

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

• Renal calculi (nephrolithiasis)

• Hypervitaminosis D

4.4 Special Warning and Precautions for Use

Overdosage

Overdose can lead to hypercalcaemia Symptoms: Anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, bone pain, nephrocalcinosis, nephrolithiasis, mental disturbances, polydipsia, polyuria and cardiac arrhythmias (severe cases). Extreme hypercalcaemia may lead to coma and death. Irreversible renal damage and soft tissue calcification may occur as a result of prolonged hypercalcaemia. Treatment of hypercalcaemia: Rehydrate and discontinue calcium supplement and any treatment with thiazide diuretics, lithium, vitamin A or D and cardiac glycosides. Monitor serum electrolytes, renal function and diuresis.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

May affect the absorption of tetracycline when used together. Concurrent use with systemic corticosteroids may reduce calcium absorption. Thiazide diuretics may decrease urinary excretion of calcium. Concurrent use with ion-exchange resins may reduce GI absorption of vitamin D. Hypercalcaemia may increase the toxicity of cardiac glycosides during treatment with calcium and vitamin D, monitor ECG and serum calcium levels. Bisphosphonate or sodium fluoride should be given at least 3 hr before calcium-containing preparations.

4.6 Pregnancy and Lactation

Pregnancy

CAL D3 PLUS Film-coated 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 of 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.

Breast-feeding

CAL D3 PLUS Film-coated 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 PLUS Film-coated Tablets have no known influence on 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 tissue disorders

Very rare: Pruritus, rash and urticaria.

Other special population

Patients with renal impairment: potential risk of hyperphosphatemia, nephrolithiasis and nephrocalcinosis.

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, polidipsia, polyuria, bone pain, nephrocalcinosis, renal calculi 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 and vitamin D must be discontinued. Treatment with thiazide diuretics and cardiac glycosides must also be discontinued. Emptying of the stomach in patients with impaired consciousness. Rehydration, and, according to severity, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids. 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

ATC Code:

Calcium Carbonate: A02AC01

Vitamin D3: A11CC

Magnesium Oxide: A02AA02

Zinc Sulphate Monohydrate: A12CB01

Calcium carbonate is used in deficiency states and as an adjunct in the prevention and treatment of osteoporosis.

Vit. D3 may have anti-osteoporotic, immunomodulatory, anticarcinogenic, antipsoriatic, antioxidant & mood-modulatory activities. Along with parathyroid hormone & calcitonin, regulate serum calcium cone.

Magnesium Oxide neutralizes gastric acid, thereby increases pH of stomach and duodenal bulb; also increases lower esophageal sphincter tone.

Zinc sulphate is used for cell growth and division, sexual maturation and reproduction, dark adaptation and night vision, wound-healing, host immunity, taste acuity, and possibly olfactory acuity.

5.2 Pharmacokinetic Properties

Calcium Carbonate

The amount of calcium absorbed through the gastrointestinal tract is approximately 30% of the swallowed dose. 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. Calcium is eliminated through faeces, urine and sweat. Renal excretion depends on glomerular filtration and calcium tubular reabsorption.

Vitamin D3

Well absorbed from the GI tract. Presence of bile is essential for adequate intestinal absorption. Bound to a specific a-globulin. Can be stored in adipose & muscle tissue for long periods of

time. Slowly released from storage sites & skin where it is formed in the presence of sunlight or uv light. May distribute into breast milk. Hydroxylated in the liver by the enzyme vitamin D 25-hydroxylase to form 25-hydroxycholecalciferol (calcifediol). Further hydroxylated in the kidneys by the enzyme vitamin D1-hydroxylase to form the active metabolites 1, 25-dihydroxycholecalciferol (calcitriol). Further metabolism also occurs in the kidneys, including the formation of the 1, 24, 25-trihydroxy derivatives. Mainly in the bile & faeces with only small amounts appearing in urine.

Magnesium Oxide

Magnesium Oxide is eliminated renally and fecally. Duration of action is 4 to 6 hours.

Zinc Sulphate

Approximately 20 to 30% of dietary zinc is absorbed, primarily from the duodenum and ileum. After absorption, zinc is bound in the intestine to the protein metallothionein. Endogenous zinc can be reabsorbed in the ileum and colon, creating an enteropancreatic circulation of zinc. Zinc is 60% bound to albumin; 30 to 40% bound to alpha-2 macroglobulin or transferrin; and 1 % bound to amino acids, primarily histidine and cysteine.

5.3 Preclinical safety data

At doses far higher than the human therapeutic range teratogenicity has been observed in animal studies. There is further no information of relevance to the safety assessment in addition to what is stated in other parts of the SPC.

6.0 Pharmaceutical Particulars

6.1 List of excipients

Tablet core:

Maize Starch	BP
Gelatin	BP
Methyl Hydroxybenzoate	BP
Propyl Hydroxybenzoate	BP
Calcium Hydrogen Phosphate	BP
Lactose	BP
Microcrystalline Cellulose	BP
Ethyl Cellulose	BP
Dichloromethane	BP
Magnesium stearate	BP
Sodium Starch Glycolate	BP
Croscarmellose Sodium	BP
Colloidal Anhydrous Silica	BP
Polysorbate-80	BP

Hydrogenated Castor Oil	BP
Purified Talc	BP
Purified Water	BP

Tablet coating:

Supercoat (SC-AQ-3076) Green	IH
Purified Tal	BP
Isopropyl Alcohol	BP
Dichloromethane	BP

6.2 Incompatibilities

Not applicable

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Store at a temperature not exceeding 25°C. Protect from light.

6.5 Nature and Contents of Container

2 x 15 tablets packed in a unit carton along with pack insert.

6.6 Special Precautions for Disposal and Other Handling

No special requirements for disposal

7.0 Registrant/Sole Agent

EMBASSY PHARMACEUTICAL & CHEMICAL LTD.

41, Ademola Street, South West Ikoyi,

Lagos, Nigeria.Tel.: 01-2900791

8. Manufacturer

LABORATE PHARMACEUTICALS INDIA LIMITED

51, Industrial Area, Gondpur, Paonta Sahib, District-Sirmour,

Himachal Pradesh (INDIA)

laborate@laborate.com

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