SUMMARY OF PRODUCT CHARACTERISTICS

1.0 NAME OF THE MEDICINAL PRODUCT:
Calcium Carbonate BP 1250 mg & Vitamin D3 BP 250 IU Tablets

2.0 QUALITATIVE AND QUANTITATIVE COMPOSITIONS:
Each uncoated chewable tablet contains:
Calcium Carbonate BP 1250 mg
equivalent to Elemental Calcium 500 mg
Colecalciferol BP 250 IU
Colour: Sunset Yellow FCF

3.0 PHARMACEUTICAL FORM
Uncoated chewable tablet

4.0 CLINICAL PARTICULARS
4.1 Therapeutic indications
Tablets should be used only as a therapeutic and not as a food supplement when the diet is deficient or when normal requirement of both components is increased.
Tablets 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.

4.2 Posology and method of administration
Adults
Adjunctive therapy in osteoporosis:
One tablet 2-3 times per day
Calcium and vitamin D deficiency:
One tablet 2-3 times per day.

Special Patient Populations
Elderly patients
Adjunctive therapy in osteoporosis
Calcium and vitamin D deficiency
Dosage as for adults.

Paediatric population
Calcium and vitamin D deficiency (only)
One tablet 1-2 times per day.

Impaired hepatic function
No dose adjustment is required.

Impaired renal function
Tablets should not be used in patients with severe renal impairment.

Method of Administration
Oral. The tablets should be chewed or sucked.

4.3 Contraindications:
Tablet is contraindicated in patients with hypersensitivity to any of the active ingredients or excipients.
- Severe renal impairment (glomerular filtration rate < 30 ml/min)
- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria
- Renal calculi (nephrolithiasis)
- Hypervitaminosis D

4.4 Special warnings and precautions for use
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.

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 metabolised 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.

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

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

Tablets contain isomalt (E953) and sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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.

If a bisphosphonate is used concomitantly, this preparation should be administered at least one hour before the intake of Tablets 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 six hours after intake of calcium.

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

Treatment with orlistat may potentially impair the absorption of fat-soluble vitamins (e.g. vitamin D_3).

4.6 Fertility, pregnancy and lactation

Pregnancy

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

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 to the child.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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); very rare (≤1/10,000) or not known (cannot be estimated from the available data).

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). Seen usually only in overdose *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 and vitamin D must be discontinued. Treatment with thiazide diuretics 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.

5. Pharmacological properties

5.1 Pharmacodynamic properties

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

ATC code: A12AX

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.

A clinical study of institutionalised patients suffering from vitamin D deficiency indicated that a daily intake of two tablets of calcium 500mg/vitamin D 250 IU for six months normalised the value of the 25-hydroxylated metabolite of vitamin D_3 and reduced secondary hyperparathyroidism and alkaline phosphatases.

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.

Cholecalciferol

Absorption: Vitamin D_3 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-hydroxycolecalciferol. It is then further converted in the kidneys to the active form 1,25-dihydroxycolecalciferol; 1,25-dihydroxycolecalciferol is the metabolite responsible for increasing calcium absorption. Vitamin D which is not metabolised is stored in adipose and muscle tissues.

Elimination: Vitamin D_3 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. There is no further information of relevance to the safety assessment in addition to what is stated in other parts of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Aspartame USPNF, Sodium Methyl Hydroxy Benzoate USPNF, Sodium Propyl Hydroxy Benzoate USPNF, Sucrose USPNF, Colour Sunset Yellow FCF Supra IH, Mannitol USP, Essence Mix fruits dry powder IH, Sodium Starch Glycolate USPNF & Purified water BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf – life:
36 months

6.4 Special precautions for storage:

Store below 30ºC. Protect from light and moisture

6.5 Nature and contents of container:
Alu PVDC Blister

7. MARKETING AUTHORIZATION HOLDER:

Cris Pharma (India) Limited
E-11, UPSIDC Industrial Area,
Selaqui, Dehradun – 248197.

8. MARKETING AUTHORIZATION NUMBER:

B4- 6414

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF AUTHORIZATION:

2ND JUNE 2016

10. DATE OF REVISION OF THE TEXT
