SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cal-D-Vita 600mg/400 IU effervescent tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One effervescent tablet contains

Calcium *as Calcium Carbonate 1500 mg*	600 mg
Cholecalciferol (Vitamin D3)	400 I.U. (equivalent to 10 microgram)

Excipients with known effect:

Aspartame (E 951)	15 mg
Sodium	98 mg
Sorbitol (E 420)	84 mg
Sucrose	20.38 mg
Soya-bean oil, partially hydrogenated	0.33 mg

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Effervescent tablet

Orange white to reddish white tablet with an odour of orange when in solution

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Prevention and treatment of combined vitamin D and calcium deficiencies in the elderly.
- Vitamin D and calcium supplementation as an adjunct to specific treatment for osteoporosis in patients with increased risk of vitamin D and calcium deficiencies

4.2 Posology and method of administration

Posology

Adults
1-2 effervescent tablets daily.Dosage in hepatic impairment
No dose adjustment is required

Dosage in renal impairment
Cal-D-Vita should not be used in patients with severe renal impairment

Method of administration

The tablets must be dissolved in at least 200 ml of water.

4.3 Contraindications

- hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- hypercalcaemia and/or conditions resulting in hypercalcaemia such as sarcoidosis, malignancy, and primary hyperthyroidism
- severe hypercalciuria
- severe renal impairment
- nephrolithiasis
- hypervitaminosis D
- hypersensitivity to soya or peanut

4.4 Special warnings and precautions for use

- The recommended dosage must not be exceeded. Overdose of calcium and vitamin D is associated with increased adverse effects including hypercalcaemia and/or hypercalciuria. Consider the dose of vitamin D (400 I.U.) when prescribing other drugs containing vitamin D. Any additional administration of vitamin D or calcium should be given under medical supervision. In such cases the serum and urinary levels of calcium must be regularly monitored.
- Cal-D-Vita contains aspartame which is metabolised to phenylalanine, which should be considered for patients with phenylketonuria
- During long-term treatment with Cal-D-Vita, the serum and urinary calcium levels should be followed and the kidney function should be monitored through measurements of serum creatinine. Monitoring is especially important in elderly patients and concomitant treatment with cardiac glycosides or diuretics. In case of hypercalcaemia or signs of impaired renal function the dose must be reduced or the treatment interrupted. It is advisable to reduce or interrupt treatment temporarily if urinary calcium exceeds 7.5 mmol/24 hours (300 mg/24 hours)(see Section 4.5).
- Milk-alkali syndrome, i.e hypercalcaemia, alkalosis and renal impairment, can develop when large amounts of calcium are ingested with absorbable alkali.
- Cal-D-Vita must be used with caution in immobilized patients, owing to an increased risk of hypercalcaemia.
- Patients with renal insufficiency have disturbed metabolism of vitamin D and if treated with cholecalciferol, the effect on calcium and phosphate homeostasis should be monitored.
- The effervescent tablet contains 84 mg sorbitol (E 420) and 20.38 mg sucrose and is, therefore, suitable for diabetics. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
- The effervescent tablet contains 98 mg sodium and, thus, can be unsuitable for patients who have been recommended a low sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Calcium

-Divalent cations such as calcium form complexes with certain substances resulting in decreased absorption of both substances. Because these interactions occur in the GI tract, taking calcium separately from other drugs should minimize the potential for interaction. It is usually sufficient to separate intake of these drugs by at least 2 hours before or 4 - 6 hours after calcium supplementation, unless otherwise specified.

Substances that form complexes include:
-Antibiotics such as tetracycline and quinolones
-Levothyroxine. Patients should take levothyroxine at least 4 hours before or 4 hours after calcium supplementation.
-Phosphates, biphosphonates and fluorides. Patients should take bisphosphonates at least 1 hour before calcium, but preferably at a different time of day.
-Eltrombopag
Calcium carbonate may interact with many substances by altering gastric pH and emptying. Because these interactions occur in the GI tract, taking calcium carbonate separately from other drugs should minimize the potential for interaction. Substances that may be affected by alterations in gastric pH with calcium carbonate include (e.g. protease inhibitors) should be administered at least 2 hours before or 1 hour after calcium carbonate.

Iron: Calcium may decrease the absorption of supplemental iron due to competitive binding. Intake of calcium and iron supplementation should be spaced at least 2 hours apart.

Calcium and/or Vitamin D:

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

-Cardiac glycosides: Hypercalcemia increases the risk of fatal cardiac arrhythmias with cardiac glycosides such as digoxin It is recommended to monitor serum calcium levels, in people taking calcium and/or vitamin D and these medications, concurrently.

Vitamin D:

-Some medication may decrease the gastro-intestinal absorption of vitamin D. Separation of intake between these medications and vitamin D by at least 2 hours before or 4-6 hours after vitamin D should minimize this interaction. Such medications include:

-Ion exchange resins (e.g. cholestyramine)

-Laxatives (e. g mineral oil, stimulant laxative such as senna)

-Orlistat

-Carbamazepine, phenytoin or barbiturates: Carbamazepine, phenytoin, or barbiturates increase metabolism of vitamin D to its inactive metabolite reducing the effect of vitamin D3

Food / Supplement interactions

Calcium:

- Oxalic acid, phytic acid: Oxalic acid, found in spinach and rhubarb, and phytic acid, found in whole cereals may inhibit calcium absorption. It is not recommended to take calcium products within 2 hours of eating foods containing high oxalic acid and phytic acid concentrations

-Iron, zinc, magnesium: Calcium supplements may decrease the absorption of dietary iron, zinc, and magnesium. This might be a factor in people at high risk for deficiency of these minerals. Patient at risk for deficiency should calcium supplements at bedtime, instead of with meals, to avoid inhibiting dietary mineral absorption.

4.6 Fertility, pregnancy and lactation

Pregnancy

During pregnancy and lactation, total daily intake from food and supplements should not exceed 1500 mg calcium and 600IU 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. Tablets can be used during pregnancy, in case of a calcium and vitamin D deficiency.

Breastfeeding

Cal-D-Vita can be used during breastfeeding.

During pregnancy and lactation, total daily intake from food and supplements should not exceed 1500 mg calcium and 600 IU vitamin D.
Vitamin D and calcium are secreted into breast milk. This must be taken into consideration if the infant is receiving any respective supplements.

Fertility

Normal endogenous levels of calcium and vitamin D are not expected to have any adverse effects on fertility

4.7 Effects on ability to drive and use machines

Cal-D-Vita has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The frequency of listed events is not known (cannot be estimated from the available data).

Gastrointestinal disorders
Gastrointestinal and abdominal pain, constipation, diarrhea, flatulence, nausea and vomiting may occur.

Immune System Disorders
Allergic reactionHypersensitivity reactions with respective laboratory and clinical manifestations include asthma syndrome, mild to moderate reactions affecting either skin, and/or respiratory tract, gastrointestinal tract and/or cardiovascular system. Symptoms may include rash, urticaria, oedema, pruritus, cardio-respiratory distress, and very rarely, severe reactions, including anaphylactic shock have been reported.

Metabolism and nutrition disorders
Hypercalcaemia and hypercalcuria (has been observed with high/excess doses)

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V*.

4.9 Overdose

Acute or long-term overdose of calcium and vitamin D, especially in suspectible patients, can cause hypervitaminosis D, hypercalcaemia, hypercalciuria, and hyperphospharemia. Consequences include renal insufficiency, vascular and soft tissue calcification including calcinosis leading to neprholithiasis.

Milk-alkali syndrome may occur in patients who ingest large amounts of calcium and absorbable alkali. Symptoms are frequent urge to urinate, continuing headache, continuing loss of appetite, nausea or vomiting, unusual tiredness or weakness, hypercalcaemia, alkalosis and renal impairment.

Uncharacteristic initial symptoms, such as abrupt onset of headache, confusion, and gastrointestinal disturbances such as constipation, diarrhea, nausea, and vomiting might be indicative of an acute overdose.

If such symptoms occur, treatment must be stopped and a health care professional consulted.

Laboratory and clinical manifestations of toxicity and hypercalcaemia are highly diverse and dependent on the patient's susceptibility and surrounding circumstances. Symptoms may include anorexia, weight loss, thirst, polyuria, and interference with the absorption of other minerals. Changes in lab values may include increase in aspartate aminotransferase and alanine aminotransferase blood concentrations. Chronic overdose can lead to calcification of vessels and organs secondary to hypercalcaemia. Extreme hypercalcaemia can result in coma and death.

Treatment

Treatment of hypercalcaemia: 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. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium, combination with other products
ATC code: A12AX

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

Vitamin D corrects an insufficient intake of vitamin D. It increases intestinal absorption of calcium. The optimal amount of vitamin D in the elderly is 500 - 1000 I.U./day.
Calcium intake corrects a lack of calcium in the diet. The commonly accepted requirement of calcium in the elderly is 1500 mg/day.
Vitamin D and calcium correct secondary senile hyperparathyroidism.

5.2 Pharmacokinetic properties

Calcium carbonate
In the stomach, calcium carbonate releases calcium ions as a function of pH. Calcium administered as calcium carbonate is absorbed to 20 - 30% and the absorption takes place mainly in the duodenum through vitamin D-dependent, saturable, active transport. Calcium is eliminated in urine, faeces and sweat. The urinary calcium excretion is a function of glomerular filtration and tubular reabsorption of calcium.

Vitamin D
Vitamin D is absorbed in the small intestine and bound to specific alpha globulins and transported to the liver where it is metabolised to 25-hydroxy-cholecalciferol. A second hydroxylation to 1, 25-dehydroxy-cholecalciferol occurs in the kidney. This metabolite is responsible for the vitamin's ability to increase the absorption of calcium. Not metabolised vitamin D is stored in tissues such as fat and muscle. Vitamin D is eliminated via faeces and urine.

5.3 Preclinical safety data

At doses far higher than 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. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol (E 420)
Aspartame (E 951)
Sucrose esters of fatty acids
Anhydrous citric acid
Sodium hydrogen carbonate
Orange flavour
Fumaric acid
Sodium chloride
β-carotene (E160a)
Beet red (E162)
Acesulfame potassium
Macrogol
Sucrose
Gelatin
Maize starch
Partially hydrogenated soybean oil
Sodium ascorbate
Medium chain triglycerides
Maltodextrine
Silicon dioxide
Acacia
All-rac-alpha-tocopherol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25^{o}C. Keep the container tightly closed in order to protect from moisture.

6.5 Nature and contents of container

Size 1x10:
Pack of one aluminium tube and a cap with integrated desiccant, containing 10 effervescent tablets.

Size 2x10:
Pack of two aluminium tubes and caps with integrated desiccant, each tube containing 10 effervescent tablets.

Size 10x10:
Pack of 10 aluminium tubes and caps with integrated desiccant, each tube containing 10 effervescent tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Bayer AB
Box 606
SE-169 26 Solna
Sweden

8. MARKETING AUTHORISATION NUMBER(S)

13383

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2015-05-13