SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

CALCI-D 1000 mg /1000 IU chewable tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains:

calcium carbonate	2500 mg (equivalent to 1000 mg calcium)
colecalciferol (Vitamin D3)	1000 I.U. (equivalent to 0.025 mg)

Excipients with known effect: sucrose, isomaltitol (E953).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Chewable tablet

The chewable tablet has a round shape and is white to almost white with a break mark.

The tablet can be divided into equal doses.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Correction of calcium and vitamin D deficiency in the elderly.

CALCI-D may be used as an adjunct to specific therapy for osteoporosis, in patients with either established vitamin D and calcium combined deficiencies or in those patients at high risk of needing such therapeutic supplements.

4.2 Posology and method of administration

Posology

Adults and elderly: 1 tablet/day for oral use

The tablets may be chewed or sucked, they should not be swallowed whole.

It is advisable to take the preparation during the evening meal.

Paediatric population: There is no relevant use of CALCI-D chewable tablets in the paediatric population.

Dosage in pregnant women: One half- tablet a day (see section 4.6).

Patients with hepatic dysfunction: No dosage adjustment is required.

Patients with renal dysfunction: CALCI-D should not be used in patients with severe renal dysfunction.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Hypercalcaemia (>10.5 mg/dl), hypercalciuria (300 mg or 7.5 mmol/24 hours), severe renal insufficiency, nephrolithiasis, nephrocalcinosus, calcification of tissues, diseases and/or conditions resulting in hypercalciurea and/or hypercalcaemia.
- Hypervitaminosis D.

4.4 Special warnings and precautions for use

- During long-term treatment it is advisable to monitor the serum and urinary calcium levels and to monitor the kidney function through measurement of serum creatinine. Monitoring is especially important in elderly patients on 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 h (300 mg/24 h).

- In patients with idiopathic infantile hypercalcaemia (e.g. CYP24A1 or SLC34A1 mutation), the risk of hypercalcaemia and secondary effects (e.g. hypercalciuria, nephrocalcinosis, nephrolithiasis) is increased due to accumulation of active vitamin D. Idiopathic infantile hypercalcaemia may be asymptomatic and undiagnosed at the beginning of vitamin D therapy and may be unmasked and become clinically apparent after vitamin D supplementation.
  Initial symptoms of hypercalcaemia are anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness and fatigue. Patient may experience polyuria resulting in dehydration and polydipsia (see section 4.9). When these symptoms occur in a patient being treated with CALCI-D, the treatment should be discontinued and the patient should be referred to a physician for evaluation and advice.
- Consider the dose of vitamin D (1000 I.U.) when prescribing other drugs containing vitamin D or food supplemented with vitamin D.
- Additional administration of vitamin D or calcium should be given under medical supervision. In such cases the plasma and urinary levels of calcium must be regularly monitored.
- Vitamin D3 may increase the magnitude of hypercalcaemia and/or hypercalciuria in patients with disease associated with unregulated overproduction of calcitriol (e.g. leukaemia, lymphoma, sarcoidosis). CALCI-D should be prescribed with caution in these patients and urine and serum calcium should be monitored.
- Patients with renal insufficiency have disturbed metabolism of vitamin D and if treated with Colecalciferol, the effect on calcium and phosphate homeostasis should be monitored. The risk of soft tissue calcification should be taken into account.
- Patients with malabsorption may not adequately absorb vitamin D
- The product should be used with caution in immobilised patients with osteoporosis due to the increased risk of hypercalcaemia. Treatment with CALCI-D could be stopped in case of prolonged immobilisation and should only be restarted after the patients has regained mobility.
- CALCI-D contains contains sucrose and isomalt (isomaltitol , E953), therefore patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. May be harmful to the teeth.
- CALCI-D contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.
- During concomitant treatment with other 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.

4.5 Interaction with other medicinal products and other forms of interaction

Absorption of orally administered tetracyclines can be reduced by the simultaneous oral administration of calcium. These two drugs should be taken at least 3 hours apart.

Treatment with orlistat may potentially impair the absorption of fat-soluble vitamins (A, D, E and K). CALCI-D should therefore be taken at least two hours after the administration of orlistat.

Some diuretics (furosemide, ethacrynic acid), antacids containing aluminium salts and thyroid hormones can inhibit calcium absorption and increase renal and faecal excretion. Thiazide diuretics can reduce urinary excretion of calcium and can induce hypercalcaemia, some antibiotics such as penicillin, neomycin and chloramphenicol can increase its absorption. Monitoring of the serum calcium levels during prolonged treatment is recommended.

Bile acid sequestrants (e.g. cholestryramine, colestipol), corticosteroids and mineral oils interfere with and reduce vitamin D absorption, while phenytoin, cimetidine and barbiturates favour its inactivation.

The calcium/digitalis synergism on the heart may cause severe disorders of cardiac function (see section 4.4).

In case of concomitant treatment with bisphosphonate or with sodium fluoride, it is advisable to allow a minimum period of three hours before taking CALCI-D (risk of reduction of the gastrointestinal absorption of bisphosphonate and sodium fluoride).

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.

Possible interactions may occur with food (e.g. foods containing phosphate, oxalic or phytinic acid) with a reduction of calcium absorption.

4.6 Fertility, pregnancy and lactation

Pregnancy

During pregnancy the daily intake should not exceed 1,500 mg calcium and 600 IU vitamin D. Studies in animals have shown reproductive toxicity of high doses of vitamin D (see section 5.3). In pregnant women, overdoses of calcium and Colecalciferol should be avoided as permanent hypercalcaemia has been related to adverse effects on the developing fetus. In addition, treatment of calcium carbonate and cholecalciferol during pregnancy, even following the recommended dosage, may unmask previous asymptomatic idiopathic infantile hypercalcaemia (e.g. CYP24A1 or SLC34A1 mutation), leading to complications related to overdose/hypercalcaemia (see section 4.4). There are no indications that vitamin D at therapeutic doses is teratogenic in humans. CALCI-D can be used during pregnancy, in case of a calcium and vitamin D deficiency.

Lactation

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

Fertility
There are no data regarding the possible effects of CALCI-D on male and female fertility.(see section 5.3).

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Undesirable effects are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100, <1/10), uncommon (≥ 1/1,000, <1/100), rare (≥ 1/10,000, <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Immune system disorders:
Not known (cannot be estimated from the available data): Serious allergic (hypersensitivity) reactions such as angioedema or laryngeal oedema.

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia and hypercalciuria
Not known (cannot be estimated from the available data): Hyperphosphatemia
Very rare: Milk-alkali syndrome (also called Burnett's syndrome and usually only seen when excessive amounts of calcium have been ingested), symptoms are 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 (see section 4.9).

Gastrointestinal disorders
Rare: Constipation, flatulence, nausea, stomach pain and diarrhoea

Skin and subcutaneous disorders
Very rare: Pruritus, rash and urticaria

Renal and urinary disorders:
Not known (cannot be estimated from the available data): Nephrolithiasis

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Overdose can lead to hypervitaminosis D and hypercalcaemia. 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.

Treatment of hypercalcaemia: the treatment with calcium and vitamin D must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A and cardiac glycosides must be also discontinued. Fluid deficiency should be balanced and individual rescue measures should be decided by the doctor. Rehydration, and, according to the 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 (electrocardiogram) and CVP (central venous pressure) should be followed.

The threshold for vitamin D intoxication is between 40,000 and 100,000 IU/day for 1-2 months in persons with normal parathyroid function, for calcium in excess of 2,000 mg per day. Symptoms of vitamin D intoxication are due to hypercalcaemia and should be treated as indicated above.

Milk-alkali syndrome may occur in patients who ingest large amounts of calcium and absorbable alkali.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium, combinations with other drugs , ATC code: A12AX

CALCI-D is a preparation for oral use, in which calcium carbonate is associated with colecalciferol (Vitamin D3).

Calcium and vitamin D have a fundamental effect on “bone rebuilding” processes and it is for this reason that they are used in those conditions of the elderly patient characterised by a negative calcium balance with low levels of circulating vitamin D and elevated serum levels of parathormone. This secondary hyperparathyroidism is effectively corrected by the combined effect of calcium carbonate and vitamin D3, the active ingredients in CALCI-D .

Vitamin D3 regulates calcium and phosphate metabolism, guaranteeing calcium absorption by the intestinal mucosa.

5.2 Pharmacokinetic properties

Approximately 30% of administered calcium is absorbed in the proximal part of the small intestine. Vitamin D is also quickly absorbed in the intestines after oral administration. The role of bile salts in facilitating absorption is well known. Approximately 40% of plasma calcium is bound to proteins, especially albumin, approximately 1/10 is diffusable, but bound to anions (phosphates); the remaining fraction is diffusable ionic calcium which has a physiological effect.

Vitamin D has a half-life of 19 to 25 hours, and circulates in the plasma bound to a specific protein, an alpha-globulin, and it is accumulated in the body for long periods. In the liver vitamin D is converted into the derivative 25-hydroxylate (calcidiol) which is put back into the circulation where it binds with a specific alpha-globulin and undergoes further hydroxylation in the kidneys into 1-25 hydroxyderivative (calcitriol). Vitamin D is excreted mainly in the bile. Only a small portion of the administered dose is found in the urine.

Calcium is secreted into the gastro-intestinal tract via the saliva, bile and pancreatic secretion. Calcium from these sources, along with the calcium that is not absorbed comprises the portion excreted in the faeces. Of the portion of calcium excreted via the renal system, approximately 2/3 of the filtered calcium is reabsorbed.

Parathormone stimulates calcium reabsorption in the convoluted distal tubules, while vitamin D increments proximal reabsorption. Part of the calcium is also excreted in perspiration.

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 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- DL-alpha tocopherol (E307)
- Medium chain triglycerides
- Modified food starch (E1450)
- Sucrose
- Sodium ascorbate (E301)
- Silicon dioxide (E551)
- Povidone K29/32
- Isomalt (E953)
- Sucralose
- Magnesium stearate
- Crospovidone
- Orange aroma

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.
Stability has been demonstrated for 14 days after first opening.

6.4 Special precautions for storage

Store below 25°C.

Store in the original package in order to protect from light and moisture.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Polypropylene tablet container with polyethylene desiccant cap.

Pack sizes of 14, 28, 42, 56, 70, 84, 98, 112, 126, 140, 154 or 168 chewable tablets packed in polypropylene tablet container. Each Polypropylene tablet container contains 14 tablets.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Consilient Health Limited,

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Dublin 2, D02 Y754,

Ireland

8 MARKETING AUTHORISATION NUMBER(S)

PL 24837/0075

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

05/08/2015

10 DATE OF REVISION OF THE TEXT

02/09/2024