Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Caltrate 500 mg / 1000 IU, chewable tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:
500 mg calcium (as calcium carbonate).
25 micrograms cholecalciferol (vitamin D_3, equivalent to 1000 IU) as cholecalciferol concentrate powder form.

Excipients with known effect:
Each chewable tablet contains 0.50 mg of aspartame (E951), 58.149 mg of sorbitol (E420), 185.00 mg of isomalt (E953), 1.925 mg of sucrose and 0.001 mg of benzyl alcohol

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Chewable, round, white tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Caltrate 500 mg / 1000 IU, chewable tablets are indicated:

- for the prevention and treatment of vitamin D and calcium deficiency in the elderly
- as vitamin D and calcium supplement as an adjunct to specific osteoporosis treatment of patients who are at risk of vitamin D and calcium deficiency.

4.2 Posology and method of administration

Posology
Adults and elderly
1 chewable tablet daily (corresponding to 500 mg of calcium and 1000 IU of vitamin D_3).

Patients with hepatic impairment
No dose adjustment is required.

Patients with renal impairment
Caltrate 500 mg / 1000 IU, chewable tablets should not be used in patients with severe renal impairment (see section 4.3).

Pregnancy
During pregnancy the daily intake should not exceed 1,500 mg of calcium and 600 I.U. of vitamin D_3. Therefore, Caltrate 500 mg / 1000 IU chewable tablets should not be used during pregnancy (see section 4.6).

Paediatric population
Caltrate 500 mg / 1000 IU, chewable tablets are not intended for use in children or adolescents (see section 4.3).

Method of administration
Oral use.

Caltrate 500 mg / 1000 IU, chewable tablets can be taken at any time, with or without food. The chewable tablets should be chewed and swallowed.
Attention should be given to a sufficient daily intake of calcium by nutrition (i.e. milk products, vegetables, mineral water).

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- Hypercalciuria and hypercalcaemia and diseases and/or conditions, which lead to hypercalcaemia and/or hypercalciuria (e.g. myeloma, bone metastases, primary hyperparathyroidism, prolonged immobilisation accompanied by hypercalciuria and/or hypercalcaemia).
- Nephrolithiasis
- Nephrocalcinosis
- Hypervitaminosis D
- Severe renal impairment

Due to its high content of vitamin D the use in children or adolescents is contra- indicated.

4.4 Special warnings and precautions for use

In the event of long-term treatment, serum calcium levels and renal function should be monitored via assaying serum creatinine. Monitoring is especially important in patients on concomitant treatment with cardiac glycosides or thiazide diuretics (see section 4.5) and in patients with a high tendency to calculus formation. In case of hypercalcaemia or signs of impaired renal function, if urinary calcium excretion exceeds 300 mg/24 hours (7.5 mmoles/24 hours) the dose should be reduced or the treatment discontinued.

Vitamin D should be used with caution in patients with impairment of 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 cholecalciferol is not metabolised normally and other forms of vitamin D should be used (see section 4.3).

Caltrate 500 mg / 1000 IU, chewable tablets should be prescribed with caution to patients suffering from sarcoidosis, due to the risk of increased metabolism of vitamin D into its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Caltrate 500 mg /1000 IU, chewable tablets should be used cautiously in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

The content of vitamin D (1000 IU) in Caltrate 500 mg / 1000 IU, chewable tablets should be considered when prescribing other medicinal products containing vitamin D or other dietary sources with a high vitamin D or calcium content (such as milk). Additional doses of calcium or vitamin D should be taken under close medical supervision. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.

Co-administration with tetracyclines or quinolones is usually not recommended or must be done with precaution (see section 4.5).
This medicinal product contains aspartame 0.5 mg in each tablet which is equivalent to 0.3 mg/g. Aspartame is a source of phenylalanine. It may be harmful for people with phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

This medicinal product contains isomalt. Patients with rare hereditary problems of fructose intolerance should not take this medicine.

This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially sodium free.

This medicine contains 58.19 mg sorbitol in each tablet which is equivalent to 33,7 mg/ g.
This medicinal product contains sucrose.

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.
This medicine contains 0.01 mg benzyl alcohol in each tablet which is equivalent to 0.006 mg/ g.
Benzyl alcohol may cause allergic reactions.
Patients are advised to ask doctor or pharmacist advice in case of pregnancy and breast feeding. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").
Patients are advised to ask doctor or pharmacist advice in case of liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").

Caltrate 500 mg / 1000 IU, chewable tablets is not intended for use in children and adolescents.

4.5 Interaction with other medicinal products and other forms of interactions

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.

Systemic corticosteroids reduce calcium absorption. Moreover, the effect of vitamin D may be decreased. During concomitant use, it may be necessary to increase the dose of Caltrate 500 mg / 1000 IU, chewable tablets.

Concomitant treatment with phenytoin or barbiturates can decrease the effect of vitamin D because of metabolic activation.

Orlistat or combined treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil may potentially reduce the gastrointestinal absorption of vitamin D. Therefore a time interval as long as possible between the intakes is recommended.

Oxalic acid (found in spinach and rhubarb) and phytic acid (found in whole cereals) may inhibit calcium absorption through formation of insoluble compounds with calcium ions. The patient should not take calcium products within two hours of eating foods high in oxalic acid and phytic acid.

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.

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 Caltrate 500 mg / 1000 IU, chewable tablets.

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, sodium fluoride or iron salts are used concomitantly, this preparation should be administered at least three hours before the intake of Caltrate 500 mg / 1000 IU, chewable 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.

4.6 Fertility, pregnancy and lactation

Pregnancy
Caltrate 500 mg / 1000 IU, chewable tablets is not recommended during pregnancy. Studies in animals have shown reproductive toxicity of high doses of vitamin D (see 5.3). 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.

Breast-feeding
Caltrate 500 mg / 1000 IU, chewable 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.

Fertility

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

4.7 Effects on ability to drive and use machines

Caltrate 500 mg / 1000 IU, chewable tablets have no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following side effects may be associated with the use of Calcium/Vitamin D and are listed under their corresponding body system organ class:
The evaluation of adverse reactions is based on the following definition of frequency:
Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <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): Hypersensitivity reactions such as angioedema or laryngeal oedema.

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia
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 (see section 4.9)

Gastrointestinal disorders
Rare: Nausea, diarrhoea, abdominal pain, constipation, flatulence, abdominal distension, eructation, vomiting

Skin and subcutaneous tissue disorders
Rare: Rash, pruritus, urticaria.

Renal and urinary disorders
Rare: Hypercalciuria, 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Overdose can lead to hypervitaminosis and hypercalcaemia. Symptoms of hypercalcaemia may include anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, mental disturbances, polydipsia, polyuria, bone pain, nephrocalcinosis, renal calculi, Nephrolithiasis, Alkalosis, hypophosphataemia, milk-alkali syndrome 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: The treatment with calcium and vitamin D must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A and cardiac glycosides must also be discontinued. Emptying of stomach in patients with impaired consciousness should be arranged. 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 (central venous pressure) should be followed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium carbonate and cholecalciferol, ATC code: A12AX01

Caltrate 500 mg / 1000 IU, chewable tablets are a fixed combination of calcium and vitamin D_3. Vitamin D_3 is involved in calcium-phosphorus metabolism. It allows the active absorption of calcium and phosphorus from the intestine and their uptake by bone. Supplementation with calcium and vitamin D_3 corrects latent vitamin D deficiency and secondary hyperparathyroidism.

5.2 Pharmacokinetic properties

Calcium
Absorption
30-40% of the ingested dose of calcium is absorbed, predominantly in the proximal part of the small intestine.

Distribution and biotransformation
99% of the calcium in the body is concentrated in the mineral component 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 5% being complexed to citrate, phosphate or other anions; the remaining 45% being bound to proteins, principally albumin.

Elimination
Calcium is excreted in the urine, faeces and in sweat. Urinary excretion depends on glomerular filtration and tubular resorption.

Vitamin D_3
Absorption
Vitamin D_3 is absorbed in the intestine.

Distribution and biotransformation
Vitamin D_3 is transported by protein binding in the blood to the liver (where it undergoes the first hydroxylation to 25-hydroxycholecalciferol) and to the kidneys (second hydroxylation to 1, 25-dihydroxycholecalciferol, the active metabolite of vitamin D_3).

Non-hydroxylated vitamin D_3 is stored in muscle and adipose tissues.

Elimination
The plasma half-life is in the order of several days; vitamin D_3 is eliminated in the faeces and urine.

5.3 Preclinical safety data

At doses far higher than the human therapeutic range teratogenicity has been observed in animal studies. No other relevant data is available that has not been mentioned elsewhere in the SmPC (see section 4.6 and 4.9).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Isomalt (E953)
Xylitol
Sorbitol (E420)
Citric acid, anhydrous
Sodium dihydrogen citrate
Magnesium stearate
Carmellose sodium

Flavour Orange "CPB" (containing flavouring substances, mannitol (E421), maltodextrin gluconolactone, sorbitol (E420))
Flavour Orange "CVT" (containing flavouring substances, mannitol (E421), gluconolactone, sorbitol (E420), medium-chained triglyceride)
Silica, colloidal hydrated
Aspartame (E951)
Acesulfam potassium
Sodium ascorbate
All-rac-alpha-tocopherol
Modified (maize) starch
Sucrose
Triglycerides, medium chain
Silicon dioxide, colloidal

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

The chewable tablets are available in strips of laminated aluminium paper foil in the following package sizes:
24, 30, 48, 60, 90, 120 chewable tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Consumer Healthcare (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0678/157/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22nd June 2018

10 DATE OF REVISION OF THE TEXT

March 2021