# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

theiCal-$D_3$ 1000 mg / 880 IU chewable tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

2,500 mg of calcium carbonate (equivalent to 1,000 mg of calcium).

8.8 mg of cholecalciferol concentrate (powder form) (equivalent to 22 micrograms ofcholecalciferol = 880 IU of vitamin $D_3$).

Excipients with known effect

Each chewable tablet contains:

- 1.00 mg of aspartame (E951)
- 119.32 mg of sorbitol (E420)
- 370.00 mg of isomalt (E953)
- 1.694 mg of sucrose
- 5.55 mg (0.24 mmol) sodium
- 0.02 mg benzyl alcohol.

For a full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Chewable tablet.

Round, white tablet with faultless surface and a breakmark.

The tablet can be divided into equal halves.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets is 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 1,000 mg of calcium and 880 IU of vitamin $D_3$).

*Dosage in hepatic impairment*

No dose adjustment is required

*Dosage in renal impairment*

Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets should not be used in patients with severe renal impairment (see section 4.3).

*Dosage during pregnancy*

During pregnancy the daily intake should not exceed 1,500 mg of calcium and 600 I.U. of vitamin $D_3$. Therefore, the daily dose must not exceed half a tablet (see section 4.6).

Method of administration

Oral use.

Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets should be taken at any time, with or without food. The chewable tablets should be chewed and swallowed.

Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets are not intended for use in children or adolescents (see section 4.3).

## 4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in 6.1.
- Hypercalciuria and hypercalcaemia and diseases and/or conditions, whichlead 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 not indicated.

## 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 measurements of 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 shouldbe 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).

Calcium Vitamin $D_3$ 1000 mg / 880 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.

Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets should be used cautiously in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

Co-administration with tetracyclines or quinolones is usually not recommended or must be done with precaution (see section 4.5).

The content of vitamin D (880 IU) in Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets should be considered when prescribing other medicinal products containing vitamin D. Additional doses of calcium or vitamin D should be takenunder close medical supervision. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.

This medicine contains 1 mg aspartame (E951) in each chewable tablet., Aspartame is a source of phenylalanine. It may be harmful for patients with phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

This medicine contains 0.02 mg benzyl alcohol in each chewable tablet. Benzyl alcohol may cause allergic reactions. Large amounts of benzyl alcohol can build-up in the body and may cause side effects (metabolic acidosis) in those who are pregnant, breast-feeding or have a liver or kidney disease.

This medicine contains less than 1 mmol sodium (23 mg) per chewable tablet, that is to say essentially ‘sodium-free’.

This medicine contains 1.694 mg sucrose in each chewable tablet. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

It also contains 119.32 mg sorbitol (E420) and 370 mg isomalt (E953) per chewable

tablet.

## 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.

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 Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets.

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

Simultaneous treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil may 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.

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 or sodium fluoride is used concomitantly, this preparation should be administered at least three hours before the intake of Calcium Vitamin $D_3$ 1000 mg / 880 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 my 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

Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets can be used during pregnancy in case of a calcium and Vitamin D deficiency. During pregnancy the daily intake should not exceed 1,500 mg of calcium and 600 I.U. of vitamin $D_3$. Therefore, the daily dose must not exceed half a tablet.

Overdoses of vitamin D have been shown to have teratogenic effects in animal experiments.

In pregnant women, overdosage of calcium and vitamin D should be avoided, since prolonged hypercalcaemia has been sometimes associated with retardation of physical and mental development, supravalvular aortic stenosis and retinopathy in the child.

Breastfeeding

Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets can be used during breast-feeding. Calcium and vitamin $D_3$ pass into the breast-milk . This should be considered when giving additional vitamin D to the child.

Fertility

No data available.

## 4.7 Effects on ability to drive and use machines

Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets has no influence on the ability to drive and use machines.

## 4.8 Undesirable effects

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, hypercalciuria.

*Gastrointestinal disorders*

Rare: Nausea, diarrhoea, abdominal pain, constipation, flatulence, abdominal distension.

*Skin and subcutaneous tissue disorders*

Rare: Rash, pruritus, urticaria.

### 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 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, vitamin D 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:

Combination of calcium with other drugs, ATC code A12AX

Mechanism of action

Calcium Vitamin $D_3$ 1000 mg / 880 IU chewable tablets is a fixed combination of calcium and vitamin $D_3$. The high calcium and vitamin $D_3$ concentration in each dose unit enables sufficient absorption of calcium with a limited number of doses. 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.

Pharmacodynamic effects

In a double-blind placebo controlled study of 18 months, including 3270 women aged 84 ± 6 and living in nursing homes, supplemented with cholecalciferol (800 IU/day) + calcium (1.2 g/day), a significant decrease in PTH secretion has been observed. After 18 months, the results of the intent to treat analysis showed 80 hip fractures in the calcium vitamin D group and 110 hip fractures in the placebo-group (p=0.004). So in the conditions of this study, the treatment of 1387 women prevented 30 hip fractures. After 36 months of follow-up, 137 women presented at least one hip fracture in the calcium-vitamin D group (n=1176) and 178 in the placebo group (n=1127) (p≤0.02).

## 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 natural orange oil concentrate, natural/nature identical mandarine oil (contains benzyl alcohol), natural/nature identical liquid flavour tropical fruit, natural/nature identical orange oil, natural/nature identical solid flavour multifruit (contains benzyl alcohol), mannitol (E421), maltodextrin, gluconolactone, sorbitol (E420))

Flavour Orange “CVT” (containing natural orange oil, natural mandarine oil, nature identical powder flavour orange, mannitol (E421), gluconolactone, sorbitol (E420), medium-chained triglyceride)

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

For tablet container:

Keep the tablet container tightly closed in order to protect from moisture.

For strips: This medicinal product does not require any special storage conditions.

## 6.5 Nature and contents of container

The chewable tablets are available in polypropylene tablet containers with polyethylene stoppers containing a desiccant in the following package sizes:

20, 28, 30, 50, 56, 60, 90, 100 (bundling package 5x20) chewable tablets

The chewable tablets are available in strips of laminated aluminium paper foil in the following package sizes:

20, 28, 30, 48, 56, 60, 90, 96, 100 (bundling package 5x20) chewable tablets

Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal

No special requirements.

# 7 MARKETING AUTHORISATION HOLDER

Stirling Anglian Pharmaceuticals Limited
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## 8 MARKETING AUTHORISATION NUMBER(S)

PL 42582/0014

## 9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

19/12/2011

## 10 DATE OF REVISION OF THE TEXT

21/07/2022