Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Calcium-D-Sandoz 600 mg + 400 IU, effervescent tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 effervescent tablet contains

1500 mg of calcium carbonate (equivalent to 600 mg or 15 mmol of calcium)

400 I.U. or 10 µg cholecalciferol (vitamin D_3) as cholecalciferol concentrate 'powder form'.

Excipient(s): 52 mg of sodium, 1.52 mg of sucrose, 50 mg of lemon flavouring (contains: sorbitol (E 420)), 0.30 mg of partially hydrogenated soybean oil

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Effervescent tablet

White-round tablet, smooth and not vaulted.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Correction of combined vitamin D_3 and calcium deficiencies.

Vitamin D_3 and calcium supplementation as an adjunct to specific treatment for osteoporosis in patients where combined calcium and vitamin D deficiencies have been diagnosed or at high risk of such deficiencies.

4.2 Posology and method of administration

Adults take 1 - 2 effervescent tablets daily (equivalent to 600-1200 mg of calcium and 400-800 I.U. of vitamin D_3). For pregnancy and lactation, see section 4.6 'Pregnancy and Lactation'.

The effervescent tablets should be dissolved in a glass of water (approx. 200 ml) and drunk immediately.

Dosage in hepatic impairment: No dose adjustment is required.

Dosage in renal impairment: Calcium-D-Sandoz should not be used in patients with severe renal impairment.

Oral use - For adults only.

4.3 Contraindications

- Hypersensitivity to the active substances, soya, peanut or to any of the excipients,
- Hypercalcaemia, hypercalciuria,
- Nephrocalcinosis, nephrolithiasis
- Disease and/or conditions resulting in hypercalcaemia and/or hypercalciuria (e.g. primary hyperparathyroidism, myeloma, bone metastases)
- Hypervitaminosis D

- Renal failure

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 the dose should be reduced or the treatment discontinued. Therapy should be reduced or preliminary interrupted, if urinary calcium level exceeds 7.5 mmol/24 h (300 mg/24 h).

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.

Calcium-D-Sandoz 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-D-Sandoz should be used cautiously in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

The content of vitamin D (400 IU) in Calcium-D-Sandoz should be considered when prescribing other medicinal products containing vitamin D. 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. Calcium and Vitamin D intake from other sources (food, dietary supplements) should be estimated, before prescribing the product.

Calcium-D-Sandoz is not intended for use in children and adolescents.

Calcium-D-Sandoz contains 2.26 mmol (corresponding to 52 mg) of sodium per tablet.

The product contains sorbitol, therefore patients with rare hereditary problems of fructose intolerance should not take this medicine.
The product contains sucrose, therefore patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Information for diabetics:
1 effervescent tablet contains 0.01 Bread Units and is therefore suitable for diabetics.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of phenytoin or other barbiturates may reduce the effect of vitamin D3 since the metabolism increases.

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. During concomitant use, it may be necessary to increase the dose of Calcium-D-Sandoz.

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 should be recommended.

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-D-Sandoz since gastrointestinal absorption of bisphosphonate may be reduced.

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.

4.6 Fertility, pregnancy and lactation

During pregnancy and lactation, combined vitamin D and calcium deficiencies can be corrected. 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 1 tablet.

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

In pregnant women, overdosage of vitamin D_3 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.

There are, however, several case reports of administration of very high vitamin D doses in hypoparathyroidism in the mother where normal children were born.

Calcium passes slightly into breast-milk, without having a negative effect on children.

Vitamin D and its metabolites also pass into breast-milk. This should be considered when giving additional vitamin D to the child.

In pregnant and lactating women, the calcium preparation should be taken at a distance of two hours from a meal due to a possible decrease of iron absorption.

4.7 Effects on ability to drive and use machines

An unfavourable effect of the preparation on the ability to drive or operate machines is very unlikely.

4.8 Undesirable effects

Immune system disorders

Very Rare (<1/10,000): Hypersensitivity reactions such as angioedema or laryngeal oedema.

Metabolism and nutrition disorders

Uncommon (>1/1,000, <1/100): hypercalcaemia, hypercalciuria.

Unknown: milk-alkali syndrome

Gastrointestinal disorders

Rare (>1/10,000, <1/1,000): nausea, diarrhea, abdominal pain, constipation, flatulence, abdominal distension.

Unknown: vomiting

Skin and subcutaneous tissue disorders

Rare (>1/10,000, <1/1,000): rash, pruritus, urticaria.

4.9 Overdose

Overdosage leads to hypervitaminosis and hypercalcaemia with the following symptoms:

Anorexia, nausea, vomiting, thirst, polydipsia, polyuria, dehydration, constipation, abdominal pain, muscle weakness, fatigue, mental disturbances, bone pain, nephrocalcinosis and in severe cases cardiac arrythmias. Extreme hypercalcemia may result in coma and death. Chronic overdosage with resulting hypercalcaemia can cause irreversible renal damage and soft tissue calcification.

The threshold for vitamin D intoxication is between 40,000 and 100,000 I.U./day for 1-2 months in persons with normal parathyroid function, for calcium in excess of 2,000 mg per day.

Treatment

In the case of an intoxication, treatment should be stopped immediately and the fluid deficiency should be balanced. Treatment with thiazide diuretics, lithium, Vitamin A 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: Mineral supplements

ATC code: Calcium, combinations with other drugs (A12AX)

Calcium-D-Sandoz is a fixed combination of calcium and vitamin D. The high calcium and vitamin D concentration in each dose unit enables sufficient absorption of calcium with a limited number of doses. Vitamin D 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. The optimal amount of Vitamin D in the elderly is 500–1000 IU/day. The commonly accepted requirement of calcium in the elderly is 1500 mg/day.

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) ($p \leq 0.02$).

5.2 Pharmacokinetic properties

Calcium carbonate:

Absorption:

On dissolution of the effervescent tablet, the calcium carbonate is converted in the presence of citric acid to soluble calcium citrate. Some 30-40% of the ingested dose of calcium is absorbed, predominantly in the proximal part of the small intestine, through Vitamin D dependant saturable active transport.

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 and 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 actual 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

No other relevant data is available that has not been mentioned elsewhere in the Summary of Product Characteristics (see 4.6 Pregnancy and lactation; 4.9 Overdose).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid anhydrous,

Malic acid,

Sodium hydrogen carbonate,

Sodium cyclamate,

Lemon flavouring (contains: lemon oil, mannitol, sorbitol, dextrin, D-glucono-1,5-lactone, acacia),

Sodium carbonate,

Maltodextrin,

Saccharin sodium,

Sucrose,

Gelatin,

Maize starch,

Partially hydrogenated soya oil,

α-tocopherol.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.

Keep the container tightly closed.

6.5 Nature and contents of container

Packs of 20, 40 (2 x 20), 60 (3 x 20) and 100 (5 packs of 20) effervescent tablets.

Each unit of 20 tablets is in an aluminium or polypropylene tube with polyethylene stopper.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

GlaxoSmithKline Consumer Healthcare (Ireland) Limited
12 Riverwalk
Citywest Business Campus
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8 MARKETING AUTHORISATION NUMBER

PA0678/128/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 14th January 2009

10 DATE OF REVISION OF THE TEXT

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