Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Kalcipos-D forte 500 mg/800 IU film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains calcium carbonate equivalent to 500 mg calcium, cholecalciferol (Vitamin D_3) 800 IU (20 microgram).

Excipients with known effect: sucrose 1.8 mg.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet. White, oval, engraved R150, 8.5 x 19 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Prevention and treatment of calcium and vitamin D deficiency in the elderly. Vitamin D and calcium supplement in addition to specific osteoporosis treatment of patients who are at risk of vitamin D and calcium deficiency.

Kalcipos-D forte film-coated tablets is indicated in adults aged 18 years and over.

4.2 Posology and method of administration

Posology
Adults and older people
One film-coated tablet (500 mg/800 IU) daily.

The amount of calcium in Kalcipos-D forte is less than the usually recommended daily intake.
Kalcipos-D forte is therefore primarily to be used by patients with need of D-vitamin substitution but with a dietary intake of calcium of 500 mg-1000 mg per day. The patients dietary intake of calcium should be estimated by the prescriber.

Patients with hepatic impairment
No dose adjustment is required

Patients with renal impairment
Kalcipos-D forte should not be used in patients with severe renal impairment (see section 4.3).

Paediatric population
There is no relevant use of Kalcipos-D forte film-coated tablets in children or adolescents.

Method of administration
Tablets shall be swallowed with water, whole, crushed or divided.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

Kalcipos-D forte film-coated tablets should be prescribed with caution to patients suffering from sarcoidosis due to 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.

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 elderly patients on concomitant treatment with cardiac glycosides or diuretics (see section 4.5) and in patients with a high tendency to calculus formation. In case of hypercalciuria (exceeding 300 mg (7.5 mmol)/24 hours) or signs of impaired renal function 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, contraindications).

Kalcipos-D forte film-coated tablets should be used cautiously in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

The content of vitamin D (800 IU) in Kalcipos-D forte film-coated tablets 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.

Milk-alkali syndrome (Burnett´s syndrome) i.e. hypercalcemia, alkalosis and renal impairment, can develop when large amounts of calcium are ingested with absorbable alkali.

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

Kalcipos-D forte film-coated tablets contains sucrose.
Kalcipos-D forte film-coated tablets contain 1.8 mg sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Sodium content
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

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.

Concomitant use of phenytoin or barbiturates may reduce the effect of vitamin D_3 since the metabolism increases.

Systemic corticosteroids reduce calcium absorption. During concomitant use, it may be necessary to increase the dose of Kalcipos-D forte.

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.

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.

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 Kalcipos-D forte.

If a bisphosphonate is used concomitantly, this preparation should be administered at least one hour before the intake of Kalcipos-D forte since gastrointestinal absorption may be reduced.

Calcium may also reduce absorption of sodium fluoride, and such preparations should be administered at least three hours before the intake of Kalcipos-D forte.

Simultaneous treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D.

Treatment with orlistat may potentially impair the absorption of fat-soluble vitamins (e.g. vitamin D_3.

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.

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.

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

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. In healthy pregnant women, the daily intake of supplemental calcium and vitamin D should not exceed 1500 mg calcium and 600 IU vitamin D.

Kalcipos-D forte is therefore not indicated for routine prophylaxis of calcium and vitamin D deficiency in pregnancy, but can be used in pregnant women who are at high risk of developing hypocalcaemia, or who already suffer from a calcium and vitamin D deficiency.

Breastfeeding
Kalcipos-D forte can be used during breastfeeding. Calcium and vitamin D_3 pass into breast milk. This should be considered when giving additional vitamin D to the child.

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

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

4.8 Undesirable effects

Adverse reactions frequencies are defined as: 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) or 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 and hypercalciuria.

Gastrointestinal disorders
Rare: Constipation, flatulence, nausea, abdominal pain, and diarrhoea.

Skin and subcutaneous tissue disorders
Rare: Pruritus, rash and urticaria.

Special populations

Patients with renal impairment are at potential risk of hyperphosphatemia, nephrolithiasis and nephrocalcinosis.

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, Website: www.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 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. 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, combinations with vitamin D and/or other drugs, ATC code: A12AX

Vitamin D increases the intestinal absorption of calcium.

Administration of calcium and vitamin D_3 counteracts the increase of parathyroid hormone (PTH) which is caused by calcium deficiency and which cause increased bone resorption.

A clinical study of institutionalised patients suffering from vitamin D deficiency indicated that a daily intake of 1000 mg calcium and 800 IU vitamin D for six months normalised the value of the 25-hydroxylated metabolite of vitamin D3 and reduced secondary hyperparathyroidism and alkaline phosphatases.

An 18 month double-blind, placebo controlled study including 3270 institutionalised women aged 84 (± 6 years) who received supplementation of vitamin D (800 IU/day) and calcium phosphate (corresponding to 1200 mg/day of elemental calcium), showed a significant decrease of PTH secretion. After 18 months, an "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).

5.2 Pharmacokinetic properties

Calcium
Absorption: The amount of calcium absorbed through the gastrointestinal tract is approximately 30% of the swallowed dose. The bioavailability of calcium can be slightly increased by concomitant intake of food.
Distribution: 99% of the calcium in the body is concentrated in the hard structure of bones and teeth. The remaining 1% is present in the intra- and extracellular fluids. Biotransformation: About 50% of the total blood-calcium content is in the physiologically active ionised form with approximately 10% being complexed to citrate, phosphate or other anions, the remaining 40% being bound to proteins, principally albumin.
Elimination: Calcium is eliminated through faeces, urine and sweat. Renal excretion depends on glomerular filtration and calcium tubular reabsorption.

Vitamin D
Absorption: Vitamin D is easily absorbed in the small intestine.
Distribution: Cholecalciferol and its metabolites circulate in the blood bound to a specific globulin. Vitamin D which is not metabolised is stored in adipose and muscle tissues.
Biotransformation: Cholecalciferol is converted in the liver by hydroxylation to the active form 25-hydroxycholecalciferol. It is then further converted in the kidneys to 1,25- dihydroxycholecalciferol. 1,25-dihydroxycholecalciferol is the metabolite responsible for increasing calcium absorption.
Elimination: Vitamin D is excreted in faeces and urine.

5.3 Preclinical safety data

At vitamin D3 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

Core:
Maltodextrin
Croscarmellose sodium
Silica, colloidal anhydrous
Magnesium stearate
Cholecalciferol concentrate:
all-*rac*-alpha-tocopherol
Sucrose
Medium chain triglycerides
Starch sodium octenyl succinate (E 1450)
Silicon dioxide
Sodium ascorbate

Coating:
Hypromellose
Macrogol
Paraffin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Store below 25°C. Store in the original package, in order to protect from light. Keep the container tightly closed in order to protect from moisture.

6.5 Nature and contents of container

20, 30, 40, 50, 60, 90, 100 and 180 tablets in plastic containers of HDPE with screw caps made of HDPE.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Mylan IRE Healthcare Limited
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8 MARKETING AUTHORISATION NUMBER

PA2010/040/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 11th May 2012
Date of Last Renewal: 20th December 2016

10 DATE OF REVISION OF THE TEXT

July 2021