Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Calcichew-D_3 Forte Chewable Tablets, calcium carbonate / colecalciferol equivalent to 500mg Calcium / 400 IU colecalciferol

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Per tablet:
Calcium carbonate 1250 mg
(equivalent to 500 mg of elemental calcium)
Colecalciferol 400 IU
(equivalent to 10 micrograms vitamin D3)
Contains sorbitol 390mg, isomalt 49.90mg, aspartame 1mg and sucrose 0.77mg.
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Chewable tablet.

Product imported from the UK
Round, white, uncoated and convex tablet. May have small specks.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Calcichew-D_3 Forte Chewable Tablets should only be used as a therapeutic supplement when the diet is deficient. It should not be used as a food supplement.

The prophylaxis and treatment of combined vitamin D and calcium deficiency particularly in housebound and institutionalised elderly subjects.

The supplementation of vitamin D and calcium as an adjunct to specific therapy for osteoporosis or as a therapeutic supplement in established osteomalacia, pregnant patients at high risk of deficiency or malnutrition when dietary intake is less than that required.

4.2 Posology and method of administration

Oral.

Adults and elderly: 2 chewable tablets per day, preferably one tablet morning and evening.

The tablet may be chewed or sucked.

Dosage in hepatic impairment:
No dose adjustment is required.

Dosage in renal impairment:
Calcichew-D_3 Forte chewable tablets should not be used in patients with severe renal impairment.

Calcichew-D_3 Forte chewable tablets are not intended for use in children.

4.3 Contraindications

- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria
- Severe renal impairment
- Nephrolithiasis
- Hypervitaminosis D
- Hypersensitivity to the active substances or to any of the excipients

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 diuretics (see section 4.5, Interactions with other medicinal products and other forms of interaction) 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.

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 colecalciferol is not metabolised normally and other forms of vitamin D should be used (see section 4.3, Contraindications).

Calcichew-D_3 Forte chewable tablets should be prescribed with caution to patients suffering from sarcoidosis due to the risk of increased metabolism of vitamin D to its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Calcichew-D_3 Forte Chewable Tablets should be used with caution in immobilised patients with osteoporosis due to the increased risk of hypercalcaemia.

The content of colecalciferol (400 IU) in Calcichew-D_3 Forte Chewable Tablets should be considered when prescribing other medicinal products containing vitamin D and/or medications or nutrients (such as milk) containing calcium.

Additional doses of calcium or vitamin D increase the risk of hypercalcaemia with subsequent kidney function impairment and milk-alkali syndrome; therefore they should be taken under close medical supervision. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.

Calcichew−D_3 Forte Chewable Tablets contain aspartame (a source of phenylalanine) which may be harmful for people with phenylketonuria.

Calcichew−D_3 Forte Chewable Tablets contain sorbitol (E420), isomalt (E953) and sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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. During concomitant use, it may be necessary to increase the dose of Calcichew-D_3 Forte Chewable Tablets.

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

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.

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 after intake of calcium.

If a bisphosphonate or sodium fluoride is used concomitantly, this preparation should be administered at least three hours before the intake of Calcichew-D_3 Forte Chewable Tablets since gastrointestinal absorption 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 calcium salts. 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
During pregnancy the daily intake should not exceed 1500 mg calcium and 600 IU colecalciferol (15µg vitamin D). Studies in animals have shown reproductive toxicity with high doses of vitamin D. 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. There are no indications that vitamin D at therapeutic doses is teratogenic in humans. Calcichew-D_3 Forte Chewable Tablets can be used during pregnancy, in case of a calcium and vitamin D deficiency.

Lactation
Calcichew-D_3 Forte Chewable Tablets can be used during breast-feeding. Calcium and vitamin D_3 pass into breast milk. This should be considered when giving additional vitamin D to the child.

4.7 Effects on ability to drive and use machines

There are no data about the effect of this product on driving capacity. An effect is, however, unlikely.

4.8 Undesirable effects

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: uncommon (>1/1,000, ≤1/100), rare (>1/10,000, ≤1/1,000) , or very rare (≤1/10,000).

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia and hypercalciuria.
Very rare: Seen usually only in overdose, see 4.9: Milk-alkali syndrome

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

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

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, polydipsia, polyuria, bone pain, nephrocalcinosis, nephrolithiasis 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 (frequent urge to urinate; continuing headache; continuing loss of appetite; nausea or vomiting; unusual tiredness or weakness; hypercalcaemia, alkalosis and renal impairment). The milk-alkali syndrome of hypercalcaemia, alkalosis and renal impairment still occur in patients who ingest large amounts of calcium and absorbable alkali; it is not uncommon as a cause of hypercalcaemia requiring hospitalisation. The syndrome has also been reported in a patient taking recommended doses of antacids containing calcium carbonate for chronic epigastric discomfort, and in a pregnant woman taking high, but not grossly excessive, doses of calcium (about 3 g of elemental calcium daily). Metastatic calcification can develop.

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. Treatment is 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 should be followed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium, combination with 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 causes increased bone resorption.

A clinical study of institutionalised patients suffering from vitamin D deficiency indicated that a daily intake of two tablets of Calcichew-D_3 Forte chewable tablets for six months normalised the value of the 25-hydroxylated metabolite of vitamin D_3 and reduced secondary hyperparathyroidism and serum alkaline phosphatase.

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). A follow-up study after 36 months showed 137 women with 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
Absorption: The amount of calcium absorbed through the gastrointestinal tract is approximately 30% of the swallowed dose.

Distribution and metabolism: 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.

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 and metabolism: Colecalciferol and its metabolites circulate in the blood bound to a specific globulin. Colecalciferol is converted in the liver by hydroxylation to the active form 25-hydroxycolecalciferol. It is then further converted in the kidneys to 1,25-hydroxycolecalciferol; 1,25-hydroxycolecalciferol is the metabolite responsible for increasing calcium absorption. Vitamin D which is not metabolised is stored in adipose and muscle tissue.

Elimination: Vitamin D is excreted in faeces and urine.

5.3 Preclinical safety data

At doses far higher than the human therapeutic range teratogenicity has been observed in animal studies. There is no further information of relevance to the safety assessment in addition to what is stated in other parts of the SmPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sorbitol (E420)
Povidone
Isomalt (E953)
Lemon flavour
Fatty acid mono- and di-glycerides
Aspartame (E951)
Magnesium stearate
Sucrose
Modified maize starch
Medium chain triglycerides
Sodium ascorbate
Anhydrous colloidal silica
Tocopherol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

The shelf life expiry date of this product shall be the date shown on the container of the product as marketed in the country of origin.

6.4 Special precautions for storage

Do not store above 30°C. Keep the container tightly closed to protect from moisture.

6.5 Nature and contents of container

White plastic bottle with tamper evident seal
Pack size: 100

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 PARALLEL PRODUCT AUTHORISATION HOLDER

Imbat Ltd
Unit L2
North Ring Business Park
Santry
Dublin 9

8 PARALLEL PRODUCT AUTHORISATION NUMBER

PPA1151/155/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28th September 2012

10 DATE OF REVISION OF THE TEXT

September 2013