Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Calcichew-D3 Forte 500 mg/400 IU Chewable Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Per tablet:

Calcium carbonate (equivalent to 500 mg of elemental calcium)	1250	mg
Colecalciferol (equivalent to 10 micrograms vitamin D_3)	400	IU

Excipients with known effect:isomalt (E953) 49.90 mg and sucrose 0.77 mg.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Chewable tablet.

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

Posology
Adults and elderly
One tablet twice daily.
Special Patient Populations
Paediatric population:
Calcichew-D_3 Forte Chewable Tablets are not intended for use in children.

Impaired hepatic function
No dose adjustment is required.
Impaired renal function
Calcichew-D_3 Forte Chewable Tablets should not be used in patients with severe renal impairment.
Method of Administration
Oral. The tablets should be chewed or sucked.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1
- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria
- Severe renal impairment (glomerular filtration rate < 30 ml/min)
- Renal calculi (nephrolithiasis)
- Hypervitaminosis D

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.

Calcichew-D_3 Forte Chewable Tablets should be used with caution in patients with hypercalcaemia or signs of impaired renal function 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).

During concomitant treatment with other high dose sources of vitamin D and/or medications or nutrients (such as milk) containing calcium, there is a risk of hypercalcaemia and milk-alkali syndrome with subsequent kidney function impairment. In these patients serum calcium levels should be followed and renal function should be monitored.

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_3 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.

Calcichew-D_3 ForteChewableTablets contain 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.

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 carbonate.
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 six hours after intake of calcium.

If a bisphosphonate is used concomitantly, this preparation should be administered at least one hour before the intake of Calcichew-D_3 Forte Chewable Tablets since gastrointestinal absorption may be reduced.

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

4.6 Fertility, pregnancy and lactation

Pregnancy
Calcichew-D_3 ForteChewableTablets can be used during pregnancy, in case of a calcium and vitamin D deficiency. During pregnancy the daily intake should not exceed 2500 mg calcium and 4000 IU vitamin D. Studies in animals have shown reproductive toxicity with high doses of vitamin D (see section 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. There are no indications that vitamin D at therapeutic doses is teratogenic in humans.

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

Calcichew-D_3 ForteChewableTablets have no known influence on the ability to drive and use machines.

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) or not known (cannot be estimated from the available data).

Immune system disorders
Not known: Hypersensitivity reactions such as angio-oedema or laryngeal oedema.

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia and hypercalciuria.
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: Constipation, dyspepsia, flatulence, nausea, abdominal pain and diarrhoea.

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

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 to 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

Symptoms
Overdose can lead to hypercalcaemia and hypervitaminosis D. 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 may occur in patients who ingest large amounts of calcium and absorbable alkali.

Treatment of hypercalcaemia
Treatment is essentially symptomatic and supportive: The treatment with calcium and vitamin D must be discontinued. Treatment with thiazide diuretics and cardiac glycosides must also be discontinued (see section 4.5). 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: Mineral supplements, Calcium, combination with vitamin D and/or other drugs

ATC code: A12AX

Vitamin D_3 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 biotransformation: 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.

Cholecalciferol
Absorption: Vitamin D is easily absorbed in the small intestine.

Distribution and biotransformation: Colecalciferol and its metabolites circulate in the blood bound to a specific globulin. Colecalciferol is converted in the liver by hydroxylation to 25-hydroxycolecalciferol. It is then further converted in the kidneys to the active form 1,25-dihydroxycolecalciferol; 1,25-dihydroxycolecalciferol is the metabolite responsible for increasing calcium absorption. Vitamin D_3 which is not metabolised is stored in adipose and muscle tissues.

Elimination: Vitamin D_3 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

Xylitol (E967)
Povidone
Isomalt (E953)
Flavouring (lemon)
Fatty acid mono- and diglycerides
Sucralose (E955)
Magnesium stearate
Sucrose
Modified maize starch
Triglycerides, medium-chain
Sodium ascorbate
Silica, colloidal anhydrous
Tocopherol

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

30 months.

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, high density polyethylene bottles.

Bottles containing 20, 30, 60, 90, or 100 tablets with tamper evident seal.

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

CHEPLAPHARM Arzneimittel GmbH
Ziegelhof 24
17489
Greifswald
Germany

8 MARKETING AUTHORISATION NUMBER

PA2239/013/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th October 1996
Date of last renewal: 04th June 2013

10 DATE OF REVISION OF THE TEXT

July 2021