SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

NATECAL D3 600mg + 400 I.U. chewable tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:

Calcium carbonate	1500 mg (equivalent to 600 mg calcium)
Cholecalciferol (Vitamin D_3)	400 I.U. (equivalent to 0.01 mg)

Excipients with known effect:
Each cheawable tablet contains 565.00 mg sorbitol (E 420), 5 mg aspartame (E 951), 67 mg lactose monohydrate, 0.3 mg partially hydrogenated soya bean oil, 1.5 mg sucrose.

This medicine contains sodium croscarmellose and saccharin sodium, sources of sodium, but less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free'.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Chewable tablet

The chewable tablet has a round, bevelled edge shape and is white to almost white with the inscription "D" on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Adults and Elderly
One tablet twice a day (e.g. one tablet in the morning and one tablet in the evening). Dose reduction should be considered as necessary following the monitoring of calcium levels as indicated in section 4.4 and 4.5.

The tablets may be chewed or sucked, they should not be swallowed whole.

The tablets should be taken preferably after meals.

Dosage in pregnant woman

One tablet a day (see section 4.6).

Dosage in hepatic impairment
No dose adjustment is required.

4.3 Contraindications

- Hypersensitivity to calcium, cholecalciferol or to any of the excipients (in particular soya bean oil)
- Kidney stones (nephrolitiasis, nephrocalcinosis)
- Severe renal impairment and renal failure
- Hypercalciuria and hypercalcaemia and diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria(e.g. myeloma, bone metastases, primary hyperparathyroidism)
- Hypervitaminosis D

4.4 Special warnings and precautions for use

- Natecal D3 tablets are not intended for children and adolescents.

- During long-term treatment it is advisable to monitor the serum and urinary calcium levels and to monitor the kidney function through measurement of serum creatinine. Monitoring is especially important in elderly patients on concomitant treatment with cardiac glycosides or diuretics. In case of hypercalcaemia or signs of impaired renal function the dose must be reduced or the treatment interrupted. It is advisable to reduce or interrupt treatment temporarily if urinary calcium exceeds 7.5 mmol/24 h (300 mg/24 h).
- Consider the dose of vitamin D (400 I.U.) when prescribing other drugs containing vitamin D or food supplemented with vitamin D.
- Additional administration of vitamin D or calcium should be given under medical supervision. In such cases the plasma and urinary levels of calcium must be regularly monitored.
- This medicine should be prescribed with caution to patients suffering from sarcoidosis, because the risk of increased metabolism of vitamin D to its active metabolite. These patients should have their urinary and plasma calcium levels monitored.
- Patients with renal insufficiency have disturbed metabolism of vitamin D and if treated with cholecalciferol, the effect on calcium and phosphate homeostasis should be monitored. The risk of soft tissue calcification should be taken into account (see section 4.8)
- This medicine should be used with caution in immobilised patients with osteoporosis due to the increased risk of hypercalcaemia.
- The calcium and alkali intake from other sources (food, dietary supplements and other drugs) should be taken into consideration when prescribing calcium supplements. If very high doses of calcium are taken concomitantly with absorbable alkali agents (like carbonate) this could lead to milk-alkali syndrome (Burnett-Syndrome), i.e. hypercalcaemia, metabolic alkalosis, renal failure and soft tissue calcification. In these cases, frequent monitoring of the calcium level in the serum and urine is necessary

<u>Excipients</u>

- This medicinal product contains aspartame, source of phenylalanine. Aspartame is hydrolysed in the gastrointestinal tract when orally ingested. It may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly. Neither non-clinical or clinical data are available to assess aspartame use in infants below 12 weeks of age.
- This medicinal product contains hydrogenated soya oil. If you re allergic to peanut or soya, do not use this medicinal product (see section 4.3).
- This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- This medicinal product contains 565,25mg sorbitol. Patients with rare hereditary problems of fructose intolerance should not take this medicine.
- This medicinal product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. May be harmful to the teeth.
- This medicinal product contains croscarmellose sodium and saccharin sodium, sources of sodium. This medicinal product contains less then 1 mmol sodium (23 mg) in each chewable tablet, that is to say essentially “sodium free”.

4.5 Interaction with other medicinal products and other forms of interaction

- Concomitant use of phenytoin or barbiturates may reduce the effect of vitamin D_3 since the metabolism increases.
- Rifampicin, may reduce the activity of vitamin D3, since it increases the rate of its metabolism
- If a biphosphonate, sodium fluoride or fluoroquinolones are used concomitantly, this preparation should be administered at least three hours before the intake of Natecal D3 since gastrointestinal absorption may be reduced.
- In case of treatment with thiazide diuretics, that reduce the renal elimination of calcium, it is recommended that the calcium levels in plasma are monitored regularly.
- Concomitant administration of glucocorticoids may decrease the effect of 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.
- Hypercalcaemia may increase the toxicity of digoxin and other cardiac glycosides during treatment with calcium and vitamin D. Patients should be monitored with regard to electrocardiogram (ECG) and serum calcium levels.
- Orlistat, combined treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D.
- Calcium salts may decrease the absorption of iron, zinc or strontium ranelate. Consequently, the iron, zinc or strontium ranelate preparation should be taken at a distance of two hours from the calcium preparation.
- Calcium salts may reduce the absorption of the estramustin or thyroid hormones. It is recommended that taking Natecal D3 be spaced at least 2 hours from these medicines.

- 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

During pregnancy the daily intake should not exceed 1,500 mg calcium and 600 IU vitamin D. Studies in animals have shown reproductive toxicity of high doses of vitamin D. In pregnant women, overdoses of calcium and cholecalciferol should be avoided as permanent hypercalcaemia has been related to adverse effects on the developing fetus. There are no indications that vitamin D at therapeutic doses is teratogenic in humans. Natecal D3 can be used during pregnancy, in case of a calcium and vitamin D deficiency.

Lactation

Natecal D3 can be used during breast-feeding. Calcium and vitamin D_3 pass into breast milk. This should be considered when given additional vitamin D to the child.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. An effect is, however, unlikely.

4.8 Undesirable effects

Undesirable effects are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100, <1/10), uncommon (≥ 1/1,000, <1/100), rare (≥ 1/10,000, <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia and hypercalciuria

Gastrointestinal disorders
Rare: Constipation, flatulence, nausea, stomach pain and diarrhoea

Skin and subcutaneous disorders
Rare: Pruritus, rash and urticaria

Immune system disorders:
Not known (cannot be estimated from the available data): Serious allergic (hypersensitivity) reactions such as angioedema or laryngeal oedema.

Other special population
Patients with renal impairment: potential risk of hyperphosphatemia, nephrolithiasis and nephrocalcinosis. See section 4.4.

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 the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

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, polidipsia, 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
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, biphosphonates, 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, combination with other drugs

ATC code: A12AX

Vitamin D corrects an insufficient intake of vitamin D. It increases intestinal absorption of calcium. The optimal amount of vitamin D in the elderly is 500-1000 I.U./day.

Calcium intake corrects a lack of calcium in the diet. The commonly accepted requirement of calcium in the elderly is 1500mg/day.

Vitamin D and calcium correct secondary senile hyperparathyroidism.

5.2 Pharmacokinetic properties

Calcium carbonate
In the stomach, calcium carbonate releases calcium ions depending upon pH. Calcium administered as calcium carbonate is absorbed to the extent of 20-30% and the absorption takes place mainly in the duodenum through vitamin D-dependent, saturable, active transport. Calcium is eliminated in urine, faeces and sweat. The urinary calcium excretion depends upon glomerular filtration and tubular reabsorption of calcium.

Vitamin D

Vitamin D is absorbed in the small intestine and bound to specific alpha globulins and transported to the liver where it is metabolised to 25-hydroxy-cholecalciferol. A second hydroxylation to 1,25-dehydroxy-cholecalciferol occurs in the kidney. This metabolite is responsible for the increase in calcium absorption. Non metabolised vitamin D is stored in tissues such as fat and muscle. Vitamin D is eliminated via 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 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

Sorbitol (E 420)
Maltodextrin
Croscarmellose sodium (E 468)
Aspartame (E 951)
Saccharin sodium (E 954)
Lactose monohydrate
Aniseed flavour (flavouring substances identical to natural substances, natural flavouring preparations, maltodextrin)
Peppermint flavour (natural flavouring preparations, maltodextrin, pulegone)
Molasses flavour (flavouring substances identical to natural substances, natural flavouring preparations, maltodextrin, triethyl citrate)
Magnesium stearate
DL-α-tocopherol (E 307)
Hydrogenated soya-bean oil
Gelatin
Sucrose
Maize starch

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years
After first opening: 60 days

6.4 Special precautions for storage

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

High density polyethylene tablet container closed with a PE cap.
The tablet container contains 12 or 60 chewable tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Chiesi Limited
333 Styal Road
Manchester
M22 5LG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 08829/0161

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/07/2007 / 22/09/2011

10 DATE OF REVISION OF THE TEXT

14/10/2021