SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Calcium D3 Nycomed 500 mg/200 IU chewable tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains:
Calcium carbonate equivalent to 500 mg calcium
Cholecalciferol concentrate (powder form) equivalent to 200 IU (5 microgram) cholecalciferol (vitamin D3)

Excipients:
Isomalt (E953)
Sucrose

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Chewable tablets with orange flavour.

Round, white and convex tablets. May have small specks.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prevention and treatment of vitamin D and calcium deficiency.
Vitamin D and calcium supplement as an adjunct to specific osteoporosis treatment of patients who are at risk of vitamin D and calcium deficiency.

4.2 Posology and method of administration

Posology

Adults and elderly
Adjunctive therapy in osteoporosis
One tablet 2-3 times per day

Calcium and vitamin D deficiency
One tablet 1-3 times per day

Paediatric population
Calcium and vitamin D deficiency (only)
One tablet 1-2 times per day.

Impaired renal function
Calcium D3 Nycomed tablets should not be used in patients with severe renal impairment (see section 4.3).

Impaired hepatic function
No dose adjustment is required.

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
- Severe renal impairment (glomerular filtration rate < 30 ml/min/1.73m^2)
- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria
- 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 measurement 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 hypercalcaemia or signs of impaired renal function the dose should be reduced or the treatment discontinued.

Calcium carbonate with cholecalciferol tablets should be used with caution in patients with hypercalcaemia or signs of impaired renal function and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account.

During concomitant treatment with other 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.

Calcium D3 Nycomed tablets should be prescribed with caution to patients suffering from sarcoidosis, due to the risk of increased metabolism of vitamin D_3 into its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Calcium D3 Nycomed tablets should be used cautiously in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

Calcium D3 Nycomed tablets 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 Interactions with other medicinal products and other forms of interaction

Thiazide diuretics reduce the urinary excretion of calcium, therefore 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.

If a bisphosphonate is used concomitantly, this preparation should be administered at least one hour before the intake of Calcium D3 Nycomed since gastrointestinal absorption may be reduced.

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.

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 Calcium D3 Nycomed.
Treatment with orlistat may potentially impair the absorption of fat-soluble vitamins (e.g. vitamin D_3).

4.6 Fertility, pregnancy and lactation

Pregnancy
Calcium D3 Nycomed 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 of 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.

Breastfeeding
Calcium D3 Nycomed 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.

4.7 Effects on ability to drive and use machines

Calcium D3 Nycomed has no known influence on 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); 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
Very rare: Pruritus, rash and urticaria.

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 national reporting system.

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, 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.
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). 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, Calcium combinations 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 calcium 500 mg/vitamin D 400 IU for six months normalised the value of the 25-hydroxylated metabolite of vitamin D_3 and reduced secondary hyperparathyroidism and alkaline phosphatases.

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 D3 is easily absorbed in the small intestine.
Distribution and biotransformation: Cholecalciferol and its metabolites circulate in the blood bound to a specific globulin. Cholecalciferol is converted in the liver by hydroxylation to 25-hydroxycholecalciferol. It is then further converted in the kidneys to the active form 1,25-dihydroxycholecalciferol. 1,25-dihydroxycholecalciferol 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 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

Xylitol (E967)
Povidone
Isomalt (E953)
Flavouring (orange)
Magnesium stearate
Sucralose (E955)
Mono- and diglycerides of fatty acids
All-rac-alpha-tocopherol
Sucrose
Modified maize starch
Triglycerides, medium-chain
Sodium ascorbate
Silica, colloidal anhydrous

6.2 Incompatibilities

Not applicable

6.3 Shelf life

High Density Polyethylene tablet container:
Pack sizes: 20,50,100, tablets: 30 months

6.4 Special precautions for storage

High Density Polyethylene tablet container: Do not store above 30°C. Keep the container tightly closed in order to protect from moisture.

6.5 Nature and contents of container

The chewable tablets are packed in:
HDPE tablet containers with HDPE/LDPE screw cap, or LDPE cap

Pack sizes: 20,50,100 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

Takeda AS
Drammensveien 852
NO-1383 Asker
Norway

8. MARKETING AUTHORISATION NUMBER(S)

15983

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of last renewal: 15.September 2016

10. DATE OF THE REVISION OF THE TEXT

19.06.2017