Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

CALVIDIN® 600 mg/400 I.U. chewable tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each chewable tablet contains:
Calcium carbonate 1500 mg
equivalent to elemental calcium 600 mg
Cholecalciferol concentrate (powder form) 4 mg
equivalent to vitamin D_3 10 µg(400 I. U.)

Excipient with known effect:
Sucrose 1,54 mg

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Chewable tablet

White biplane tablets with a snap grove and the letters C/D.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Correction of combined vitamin D and calcium deficiencies in the elderly.
Supply of vitamin D and calcium as an adjunct to specific treatments for osteoporosis, in patients where combined vitamin D and calcium deficiencies have been diagnosed or those at a high risk of such deficiency.

CALVIDIN® is indicated in adults aged 18 years and over.

4.2 Posology and method of administration

Posology
Adults and elderly
One chewable tablet twice a day [e. g. one tablet in the morning and one tablet in the evening (equivalent to 1200 mg of calcium and 800 I.U. of vitamin D_3)]. Dose reduction should be considered as necessary following the monitoring of calcium levels as indicated in section 4.4 and 4.5.

Pregnant women
One chewable tablet a day (see section 4.6).

Paediatric population
There is no relevant use of CALVIDIN® in children or adolescents.

Posology in cases of hepatic insufficiency
The dose does not require adjustment.

Posology in cases of renal insufficiency
Dosage in renal impairment: CALVIDIN® chewable tablets should not be used in patients with severe renal impairment.

Method of administration
The tablets are chewed and then swallowed with a little liquid.
In exceptional cases (e.g. patients disabled) the tablets can, after consulting a doctor, be sucked.

4.3 Contraindications

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

4.4 Special warnings and precautions for use

In the event of prolonged treatment, checking calcaemia and renal function by assaying serum creatinine is justified. This monitoring is particularly important in the elderly, in cases of combined treatment with cardiac glycosides and diuretics (see section 4.5) and in patients who are frequently subject to the formation of kidney stones. In the presence of hypercalcaemia or signs of problems with renal function the dose must be reduced or treatment interrupted. Therapy should be reduced or preliminary interrupted if urinary calcium level exceeds 7.5 mmol/24 hours (300 mg/24 hours).

CALVIDIN® chewable tablets must be prescribed with caution to patients who are immobilized and suffering from osteoporosis, because of the increase in the risk of hypercalcaemia.

Take into account the intake of vitamin D, calcium and alkali like carbonate from all other sources (e.g. dietary supplements or food) before prescribing CALVIDIN® chewable tablets. As these products already contain vitamin D and calcium carbonate, the additional administration of vitamin D or calcium carbonate may lead to a Burnett Syndrome (hypercalcaemia, metabolic alkalosis, renal failure and soft tissue calcification) and must therefore be carried out under strict medical supervision with regular monitoring of calcaemia and calciuria.

CALVIDIN® chewable tablets must be used with caution in patients suffering from sarcoidosis because of a possible increase in vitamin D_3 metabolism to its active form. In these patients, calcaemia and calciuria must be monitored.

CALVIDIN® chewable tablets must be used with caution and phosphate-calcium levels monitored in patients presenting with a decrease in renal function. The risk of soft tissue calcification must be taken into account. In patients with severe renal insufficiency vitamin D_3 in the form of cholecalciferol is not metabolized in the normal way and other forms of vitamin D_3 must be used (see section 4.3).

CALVIDIN® chewable tablets is not intended for use in children or adolescents.

Excipients
This product contains sucrose, therefore patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. May be harmful to teeth.

Note for diabetics:
The proportion of digestible carbohydrate in CALVIDIN® chewable tablets is 0.47 g per tablet. The daily dose of 2 tablets corresponds to 0.08 carbohydrate units (CU).

Sodium
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 calcium excretion in the urine. Because of the increased risk of hypercalcaemia, calcium monitoring is recommended in cases when thiazide diuretics are given simultaneously.

Systemic corticosteroids reduce calcium absorption. In the case of concomitant administration of corticosteroids, it might be necessary to increase the dose of CALVIDIN ® chewable tablets.

Orlistat, combined ion-exchange resin treatment such as cholestyramine or laxatives such as paraffin oil can reduce the gastrointestinal absorption of vitamin D_3. An interval of at least two hours should be observed between ingestion of ion-exchange resins (e. g. cholestyramine) or laxatives and CALVIDIN® chewable tablets as otherwise the absorption of vitamin D_3 is reduced.

Calcium carbonate can alter tetracycline absorption when given simultaneously. It is recommended that taking tetracycline be staggered by at least 2 hours before or 4 to 6 hours after taking calcium by mouth.

Hypercalcaemia can increase the toxicity of cardiac glycosides in the case of simultaneous administration with calcium and vitamin D. Consequently patients must be monitored regularly (ECG check and calcaemia).

Rifampicin, phenytoin or barbiturates may reduce the activity of vitamin D_3, since they increase the rate of its metabolism.

Calcium salts may decrease the absorption of iron, zinc or strontium. Consequently, the iron, zinc or strontium 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 CALVIDIN ® chewable tablets be spaced at least 2 hours from these medicines.

In the case of concomitant bisphosphonate, sodium fluoride or fluoroquinolone administration, it is recommended that taking CALVIDIN ® chewable tablets be spaced by at least 3 hours, as their absorption during digestion may be reduced.

Oxalic acid (found in spinach and rhubarb) and phytic acid (found in wholegrain cereals) can inhibit calcium absorption by forming insoluble compound with calcium ions. Patients must not take calcium containing-products in the two hours after the consumption of foods rich in oxalic acid and phytic acid.

4.6 Fertility, pregnancy and lactation

Pregnancy
CALVIDIN® chewable tablets may be given during pregnancy in cases of calcium and vitamin D_3 deficiency.

During pregnancy the daily dose should not exceed 1500 mg of calcium and 600 I.U. of vitamin D. Therefore the daily dose must not exceed 1 tablet.
Animal studies have shown toxic effects on reproduction at high doses of vitamin D. In pregnant women, all calcium or vitamin D overdoses must be avoided, as prolonged hypercalcaemia in pregnancy may lead to retardation of physical and mental development, supravalvular aortic stenosis and retinopathy in the child. There are no indications that Vitamin D_3 at therapeutic doses is teratogenic in man.

Breastfeeding
CALVIDIN® chewable tablets can be used during breastfeeding. Calcium and Vitamin D_3 pass into maternal milk. This must be taken into consideration when vitamin D_3 is given concomitantly to the child.

In pregnant and lactating women, the calcium preparation should be taken at a distance of two hours from a meal due to a possible decrease of iron absorption.

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

CALVIDIN® has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The evaluation of undesirable effects is generally based on the following frequency convention:
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), 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 angiooedema or laryngeal oedema

Metabolism and nutrition disorders
Uncommon (≥ 1/1,000 to < 1/100): Hypercalcaemia and hypercalciuria

Gastrointestinal disorders
Rare (≥ 1/10,000 to < 1/1,000): Constipation, flatulence, bloating, abdominal distension, nausea, abdominal pain, diarrhoea
Not known (cannot be estimated from the available data): Vomiting

Skin and subcutaneous tissue disorders
Rare (≥ 1/10,000 to < 1/1,000): Pruritus, rash and urticaria

Patients with renal impairment have a potential risk for the adverse events of hyperphosphataemia, 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

An overdose can lead to hypervitaminosis and hypercalcaemia. The symptoms of hypercalcaemia can include: anorexia, thirst, nausea, vomiting, constipation, dehydratation, abdominal pain, muscle weakness, fatigue, mental disturbances, polydipsia, polyuria, skeletal pain, renal calcinosis, kidney stones and in severe cases cardiac arrhythmia. Extreme hypercalcaemia may lead to coma and death. Continuous high calcium levels may lead to irreversible damage to the kidneys and soft tissue calcification.
Treatment of hypercalcaemia: All calcium and vitamin D_3 treatments must be stopped. Treatment with thiazide diuretics, lithium, vitamin A and cardiac glycosides must also be stopped. Gastric lavage should be performed on patients with problems affecting consciousness.
Rehydrate and, depending on severity, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids should be considered. Serum electrolytes, kidneyfunction and diuresis must be monitored. In severe cases ECG and calcaemia should be monitored.
The threshold for vitamin D intoxication is between 40,000 and 100,000 I. U./day for 1-2 months in persons with normal parathyroid function, for calcium in excess of 2,000 mg per day.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium combination with vitamin D and/or other drugs.
ATC code: A12AX

Vitamin D supplementation corrects an insufficient vitamin D intake. It increases the intestinal absorption of calcium. The optimal vitamin D dose in elderly subjects is 500 - 1000 I.U. per day. Calcium supplementation balances a dietary calcium deficiency. The usual calcium requirement of the elderly is 1500 mg/day. Vitamin D and calcium supplementation correct secondary senile hyperparathyroidism.

An 18 months, double-blind, placebo-controlled study carried out in 3270 women living in institutions, aged 84±6 years and receiving a vitamin D_3 supplement (800 I.U./day) and calcium phosphate (corresponding to
1200 m g/day of elemental calcium) showed a significant decrease in PTH secretion. After 18 months, following an "intention to treat" (ITT) analysis 80 hip fractures were observed in the calcium vitamin D_3 group and 110 hip fractures in the placebo group

(p=0.004). In a follow-up study after 36 months, 137 women with at least one fracture of the hip were observed in the calcium vitamin D_3 group (n=1176) versus 178 in the placebo group (n=1127) ($p \leq 0.02$).

5.2 Pharmacokinetic properties

Calcium
Absorption:
In the stomach, calcium carbonate releases calcium ions depending upon pH. The amount of Calcium absorbed by the gastrointestinal tract is in the order of 30% of the ingested dose.
Distribution and biotransformation:
99% of calcium is stored in the hard matter of bones and teeth. The remaining one percent is found in intra and extracellular liquids. Approximately 50% of total blood calcium is found in the physiologically active ionised form, of which approximately 10% in complexes with citrate, phosphate or other anions with 40% remaining bound to proteins, mainly albumin.
Elimination:
Calcium is eliminated in the urine, faeces and in the sweat. Kidney excretion depends on glomerular filtration and calcium reabsorption by the tubules.
Vitamin D

Absorption:
Vitamin D is easily absorbed by the small intestine.

Distribution and biotransformation:
Cholecalciferol and its metabolites circulate in the blood, linked to a specific alpha globulin. Cholecalciferol is metabolised in the liver by hydroxylation to its active form, 25-hydroxycholecalciferol. It is then metabolised in the kidneys to 1,25-dihydroxycholecalciferol. 1,25-dihydroxycholecalciferol is the metabolite responsible for the increase in calcium absorption. The vitamin D_3 that is not metabolised is stored in adipose and muscle tissue.

Elimination
Vitamin D_3 is excreted via the faeces and urine.
The plasma half-life is in the order of several days.

5.3 Preclinical safety data

A teratogenic effect has been observed in animal studies at very much higher doses than human therapeutic doses.

There is no further 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
Mannitol (E421)
Magnesium stearate
Silica colloidal anhydrous
Pregelatinised maize starch
Butylated hydroxytoluene (E321)
Triglycerides medium-chain
Sucrose
Gelatin
Modified maize starch
Sodium aluminium silicate
Flavouring agents (Tutti frutti Givaudan: allylhexanoate, amylbutyrate, citronellol, ethylacetate, ethylbutyrate, ethylvanillin, geraniol, β-ionone, α-ionone, isoamylacetate, maltodextrin, modified starch, propylenglycol)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

30 months.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

PVC/PVDC/Aluminium blisters, each containing 10 chewable tablets.
Cardboard box containing 20, 30, 50, 60, 100, 300 chewable tablets.
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

PA2010/038/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of latest renewal: 4th August 2009

10 DATE OF REVISION OF THE TEXT

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