SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME
CALCIFORTE VITAMIN D3, tablet to be chewed, sucked or dispersed.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Elemental calcium .....500.00 mg
In the form of calcium carbonate .....1250.00 mg
Cholecalciferol or vitamin D3..... 400 IU
In the form of cholecalciferol concentrate, powder form
Saccharomyces cerevisiae yeast .....50.00 mg

per a tablet

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM: Tablet to be chewed, sucked or dispersed.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

- Correction of vitamin and calcium deficiencies in the elderly.
- Intake of vitamin and calcium in combination with specific treatments for osteoporosis in deficient patients or patients at high risk of calcium and vitamin D deficiency.

4.2 Posology and method of administration
Oral route. **For adults only.**
The daily dosage is 2 tablets daily i.e. 1 tablet morning and night.
The tablets are to be chewed, sucked or dispersed.

4.3. Contraindications
This medicine is contra-indicated in case of:
- hypersensitivity to one of the ingredients,
- hypercalcaemia, hypercalciuria, calcium calculus,
- prolonged immobilisation accompanied by hypercalciuria and/or hypercalcaemia: vitamin and calcium treatment is only to be initiated after resumption of mobility,
- phenylketonuria (due to the presence of aspartame).

4.4. Special warnings and precautions for use

<u>Precautions for use</u>

- In the event of long-duration treatment, it is appropriate to control calciuria and reduce or interrupt temporarily treatment if calciuria exceeds 7.5 mmol/24 h (300 mg/24 h).
- In the event of concomitant treatment with digitalis, bisphosphonates, thiazide diuretics, cyclines, iron salts or estramustine: see section 4.5
- Take the dose of vitamin D per tablet (400 IU) into account together with any other prescription of vitamin D. Since this product already contains vitamin D, supplementary administration of vitamin D or calcium is to be conducted under strict medical monitoring with weekly control of calcaemia and calciuria.
- The product is to be prescribed with caution for patients presenting with sarcoidosis due to the possible increase of metabolism of vitamin D in its active form.
In those patients, calcaemia and calciuria are to be monitored.

- The product is to be used with caution in patients with renal failure and the phosphate/calcium balance is to be monitored.
- Due to the presence of sorbitol, this medicine is not to be used in the event of fructose intolerance.
- Due to the presence of sucrose, this medicine is contra-indicated in the event of fructose intolerance, glucose-galactose malabsorption syndrome and sucrase-isomaltase deficiency.

4.5. Interactions with other medicinal products and other forms of interactions

Combinations being the object of precautions for use:
+ Cyclines:
Decrease in the digestive absorption of cyclines.
Take the calcium salts remotely from the cyclines (more than 2 hours if possible)
+ **Digitalis:**
Risk of arrhythmia.
Clinical monitoring and, if appropriate, control of the ECG and serum calcium.
+ Bisphosphonates:
Risk of decreased digestive absorption of bisphosphonates.
Take the calcium salts remotely from the bisphosphonates (more than 2 hours if possible)
+Estramustine:
Decrease in the digestive absorption of estramustine.
Take the calcium salts remotely from estramustine (more than 2 hours if possible).
+ Iron (salts) (oral route):
Decreased digestive absorption of iron salts.
Take the iron remotely from meals and in the absence of calcium.

Combinations to be taken into account:
+ Thiazide diuretics:
Risk of hypercalcaemia due to decreased urinary excretion of calcium.

4.6.Pregnancy and lactation
This product may be used during pregnancy and lactation. However, the daily dose is not to exceed 1500 mg of calcium and 600 IU of vitamin D3.
During pregnancy, cholecalciferol overdose is to be avoided:
- Vitamin D overdose during gestation had teratogenic effects in animals.
- In pregnant women, vitamin D overdose is to be avoided since permanent hypercalcaemia may induce physical and mental retardation in the child, supra-valve aortic stenosis and retinopathy. However, several children have been born without any malformation following administration of very high doses of vitamin D3 for maternal hypoparathyroidism.

- Vitamin D and its metabolites are excreted in breast milk.

4.7. Effects on ability to drive and use machines: Not applicable

4.8. Adverse effects
- Constipation, flatulence, nausea, epigastric pain, diarrhoea.
- Hypercalciuria and, exceptionally, hypercalcaemia in the event of prolonged high-dose treatment.
- Risk of the occurrence of hypersensitivity reaction (anaphylactic shock, urticaria) due to the presence of soy proteins.
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 Agence nationale de sécurité du medicament et des produits de santé (ANSM) in the network of the Regional Centres of Pharmacovigilance – Website: www.ansm.sante.fr

4.9. Overdose
Acute overdose gives rise to hypercalciuria and hypercalcaemia whose symptoms are as follows: nausea, vomiting, polydipsia, polyuria, constipation.
Chronic vitamin D3 overdose may induce vascular and tissue calcifications due to the hypercalcaemia.

Treatment:
Discontinue all calcium and vitamin D intake; rehydration.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic class: **MINERAL SUPPLEMENTS**

ATC code**: A12AX**
(A: gastrointestinal system and metabolism)

The vitamin D corrects the insufficient intake of vitamin D.
Vitamin D increases the intestinal absorption of calcium and calcium binding to osteoid tissue.
The calcium intake corrects the dietary calcium deficiency.

The daily calcium requirements are of the order of 1000 to 1500 mg of elemental calcium and 500 to 1000 IU/day of vitamin D.

Vitamin D and calcium correct secondary senile hyperparathyroidism.

A double-blind, placebo-controlled study of duration 18 months included 3270 women aged 84 $\pm$ 6 years living in care centres and showed a significant decrease in plasma PTH levels. At 18 months, the results of the intent-to-treat analysis showed 80 hip fractures in the calcium-vitamin D group and 110 hip fractures in the placebo group ($p = 0.004$).
Under the study conditions, treatment of 1387 women prevented 30 hip fractures. After prolongation to 36 months, the following results were obtained: 137 hip fractures in the calcium-vitamin D group and 178 in the placebo group ($p \leq 0.02$).

5.2. Pharmacokinetic properties

Calcium carbonate
In the gastric medium, calcium carbonate releases the calcium ion according to pH.
Calcium is essentially absorbed in the proximal small intestine.
The gastrointestinal absorption rate is of the order of 30% of the dose ingested.
Calcium is excreted in sweat and digestive secretions.
Urinary calcium depends on glomerular filtration and the rate of tubule reabsorption of calcium.

Vitamin D3
Vitamin D3 is absorbed from the intestine and, after protein binding, transported into the blood to the liver (first hydroxylation) and kidneys (second hydroxylation).
Non-hydroxylated vitamin D3 is stored in reserve compartments such as adipose tissue and muscles.
The plasma half-life is of the order of a few days. Vitamin D3 is excreted in the faeces and urine.

5.3. Preclinical safety data: Not applicable

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6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Pregelatinised starch, sorbitol, glycerol dibehenate, croscarmellose sodium, aspartame, powdered orange flavour (maltodextrin, soy proteins, gum arabic, concentrated orange juice, essential oil of orange, essential oil of lemon, citral, acetaldehyde, linalol, ethyl butyrate, alpha-terpineol, octanal, ethyl acetate, geranyl acetate).

Coating of the cholecalciferol concentrate: alpha-tocopherol, dietary fats, gelatine, sucrose, maize starch.

6.2. Incompatibilities: Not applicable.

6.3 Shelf life

18 months.

6.4. Special precautions for storage: Store at a temperature not exceeding 25°C.

6.5. Nature and contents of container: 60 or 180 tablets in heat-formed blister packs (PVC + PVDC + aluminium).

6.6. Special precautions for disposal: No special requirements.

7. MARKETING AUTHORISATION HOLDER: Laboratoires GRIMBERG **-** 19, rue Poliveau **-** 75005 Paris - France

8. MARKETING AUTHORISATION NUMBER(S)

356 682-5 or 34009 356 682 5 7: 60 tablets in heat-formed blister packs (PVC+PVDC+aluminium.)
373 774-1 or 34009 373 774 1 6: 180 tablets in heat-formed blister packs (PVC+PVDC+aluminium.)

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION: 04/12/2006

10. DATE OF REVISION OF THE TEXT: 18/02/2010

PRESCRIBING AND DISPENSING CONDITIONS

Medicinal product not subject to medical prescription.