SUMMARY OF PRODUCT CHARACTERISTICS

NAME
CALCIFORTE VITAMIN D3, chewable, suckable or dispersible tablet

QUALITATIVE AND QUANTITATIVE COMPOSITION

Elemental calcium	500.00 mg
In the form of calcium carbonate	1250.00 mg
Cholecalciferol or vitamin D3	400.00 IU
In the form of cholecalciferol concentrate, powder form	
Saccharomyces cerevisiae yeast	50.00 mg

per a tablet of 2.015g

Excipients with known effects: aspartam, sorbitol, saccharose, soy protein.

For a full list of excipients, see section “List of excipients”.

PHARMACEUTICAL FORM

Chewable, suckable or dispersible tablet.

CLINICAL PARTICULARS

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.

Posology and method of administration

Posology
Oral route. For adults only.
The daily dosage is 2 tablets daily i.e. 1 tablet morning and night.

Method of administration
Chewable, suckable or dispersible tablet.
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 aspartam),
- peanuts or soy allergy

Special warnings and precautions for use

Precautions for use

- In cases 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 case of concomitant treatment with cyclin, digoxin, bisphosophonate, estramustine, iron salts, thyroid hormones, strontium, zinc, rifampicin, ciprofloxacin, norfloxacin, integrase inhibitors, enzyme-inducing anticonvulsants, orlistat and thiazide diuretics: see section “Interactions with other medicinal products and other forms of interactions”.
- Take into account the supply of vitamin D per tablet (400 IU) 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. Calcaemia and calciuria should be monitored in these patients.
- The product should be used with caution in patients with renal impairment with monitoring of the phosphocalcic balance.
- This medicine contains 381,0 mg of sorbitol per tablet. Patients with hereditary fructose intolerance (HFI) should not take or receive this medicinal product.
- This medicine contains 10.0 mg of aspartam per tablet. .Aspartam is a source of phenylalanine. 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.
- This medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
- This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

Interactions with other medicinal products and other forms of interactions

Combinations being the object of precautions for use:

+ Cyclin:
Decrease in the digestive absorption of cyclines.
Take the calcium salts remotely from the cyclines (more than 2 hours if possible)

+ **Digoxin:**
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 (from at least 30 minutes to more than 2 hours if possible depending on a bisphosphonatel)

+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.

+ Thyroid hormones:
Decreased digestive absorption of thyroid hormones.
Take calcium salts away from thyroid hormones (more than 2 hours, if possible).

+ Strontium:
With calcium salts administered orally: decreased digestive absorption of strontium.
Take strontium away from calcium salts (more than 2 hours, if possible).

+ Zinc:
Decreased digestive absorption of zinc by calcium.

Take calcium salts away from zinc (more than 2 hours, if possible).

+ Rifampicin:
Decrease in vitamin D concentrations greater than without treatment with rifampicin.
Determination of vitamin D concentrations and supplementation if necessary.

+ Ciprofloxacin
Decreased digestive absorption of ciprofloxacin.
Take calcium salts away from ciprofloxacin (more than 2 hours, if possible).

+ Norfloxacin
Decreased digestive absorption of norfloxacin.
Take calcium salts away from norfloxacin (more than 2 hours, if possible).

+ Integrase inhibitors
Decreased digestive absorption of integrase inhibitors.
Take calcium salts away from the antiretroviral (more than 2 hours, if possible).

+ Enzyme-inducing anticonvulsants:
Decrease in vitamin D concentrations more apparent than without the inducer.
Determination of vitamin D concentrations and supplementation if necessary.

Combinations to be taken into account:

+ Thiazide diuretics:
Risk of hypercalcaemia due to decreased urinary excretion of calcium.

+ Orlistat:
Decreased absorption of vitamin D.

Fertility, pregnancy and breast-feeding
Pregnancy
This product may be used during pregnancy. However, the daily dose must not 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.

Breast-feeding
This product may be used during breast-feeding. However, the daily dose must not exceed 1500 mg of calcium and 600 IU of vitamin D3.
- Vitamin D and its metabolites are excreted in breast milk.

Undesirable effects

- Constipation, flatulence, nausea, epigastric pain, diarrhoea.
- Hypercalciuria and, exceptionally, hypercalcaemia in the event of prolonged high-dose treatment.
- Pruritus, skin rash, urticaria;
- Risk of the occurrence of hypersensitivity reaction (anaphylactic shock, urticaria) due to the presence of soy proteins.

Reporting of suspected undesirable effects
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.signalement-sante.gouv.fr

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:
Discontinuation of all calcium and vitamin D intake; rehydration.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Pharmacotherapeutic class: MINERAL SUPPLEMENTS - ATC code: A12AX

Mechanism of action

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 around 1000 to 1500 mg of elemental calcium and 500 to 1000 IU/day of vitamin D.
Vitamin D and calcium correct secondary senile hyperparathyroidism.

Clinical efficacy and safety

A 18-month double-blind, placebo-controlled study 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 ($p \leq 0.02$).

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 around 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.

PHARMACEUTICAL PARTICULARS

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.

Shelf life

2 years.

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

Nature and contents of external container
Tablets in heat-formed blister packs (PVC/PVDC/Aluminium). Box of 60 or 180.

Special precautions for disposal and other handling
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

MARKETING AUTHORISATION HOLDER:

Laboratoires GRIMBERG SA – 44 avenue Georges Pompidou- 92300 Levallois-Perret - France

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)

DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION:
17 April 2001/10 March 2015

DATE OF REVISION OF THE TEXT: 16 December 2020

PRESCRIBING AND DISPENSING CONDITIONS

Medicinal product is not subject to medical prescription.