IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0170/018/001
Case No: 2046809

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Procter & Gamble Pharmaceuticals

Rusham Park, **Whitehall Lane**, **Egham**, **Surrey TW20 9NW**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Cacit D3 500 mg / 440 IU, Effervescent Granules for Oral Solution.

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **04/07/2008**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cacit D3 500 mg / 440 IU, Effervescent Granules for Oral Solution.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One sachet of 4 g contains :

Calcium carbonate		1250.0	mg
equivalent to calcium element	500	mg or 12.5	mmol
Colecalciferol concentrate (powder form)		440.0	IU
equivalent to colecalciferol (Vitamin D_3)		11.0	µg

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Effervescent white granules for oral solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Correction of vitamin D and calcium combined deficiency in elderly people.

Vitamin D and calcium supplementation as an adjunct to specific therapy for osteoporosis treatment in patients with established, or at high risk of vitamin D and calcium combined deficiencies.

4.2 Posology and method of administration

Posology

One or two sachets per day.

Method of administration

Oral.

Pour the contents of the sachet into a glass, add a large quantity of water, then drink immediately.

4.3 Contraindications

- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria.
- Nephrolithiasis.
- Hypervitaminosis D.
- Hypersensitivity to the active substances or to any of the excipients (in particular soya oil).

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 measurements 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.

Vitamin D should be used with caution in patients with impairment of renal function and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account. In patients with severe renal insufficiency, vitamin D in the form of cholecalciferol is not metabolised normally and other forms of vitamin D should be used (see Section 4.3, Contraindications)

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

Cacit Vitamin D3 sachets should be used cautiously in immobilised patients with osteoporosis due to the increased risk of hypercalcaemia.

The content of vitamin D (440 IU) in Cacit Vitamin D3 sachets should be considered when prescribing other medicinal products containing vitamin D. Additional doses of calcium or vitamin D should be taken under close medical supervision. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.

Cacit Vitamin D3 sachets are not intended for use in children**.**

Special warnings

Cacit Vitamin D3 sachets contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use requiring precautions:

- Digitalis and other cardiac glycosides: the oral administration of calcium combined with vitamin D increases the toxicity of digitalis (risk of dysrythmia). Strict medical supervision, and if necessary, monitoring ECG and calcaemia are necessary.
- Bisphosphonate, sodium fluoride: it is advisable to allow a minimum period of two hours before taking the calcium (risk of reduction of the gastrointestinal absorption of bisphosphonate and sodium fluoride).
- Thiazide diuretics: reduce urinary elimination of calcium therefore supervision of calcaemia is recommended.
- Phenytoin or barbiturates: can decrease the effect of vitamin D because of metabolic inactivation.
- Glucocorticosteroid: can decrease the effect of vitamin D.
- Tetracyclines by oral route: it is advisable to delay taking the calcium by at least three hours (calcium salts reduce the absorption of tetracyclines).
- Possible interactions with food (e.g. containing oxalic acid, phosphate or phytinic acid).

4.6 Pregnancy and lactation

The product may be used during pregnancy and lactation. However, the daily intake should not exceed 1500 mg calcium and 600 IU vitamin D3.

In pregnancy, overdoses of colecalciferol must be avoided.

Overdoses of vitamin D have shown teratogenic effects in pregnant animals.

In humans, overdoses of colecalciferol must be avoided as permanent hypercalcaemia can lead to physical and mental retardation, supravalvular aortic stenosis and retinopathy in the child.

There are however several case reports of administration of very high doses in hypoparathyroidism in the mother, where normal children were born.

Vitamin D and its metabolites pass into the breast milk.

4.7 Effects on ability to drive and use machines

No remarkable findings. No effect expected.

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) or rare (>1/10,000, <1/1,000).

Metabolism and nutrition disorders
Uncommon : Hypercalcaemia and hypercalciuria.

Gastrointestinal disorders
Rare : Constipation, flatulence, nausea, abdominal pain and diarrhoea.

Skin and subcutaneous disorders
Rare : Pruritus, rash and urticaria.

4.9 Overdose

Consequence of overdose are hypercalciuria and hypercalcaemia. Symptoms includes: nausea, vomiting, thirst, polydipsia, polyuria, constipation.

Chronic overdoses can lead to vascular and organ calcifications as a result of hypercalcaemia.

Treatment

Stop all intake of calcium and vitamin D, rehydration.

5 PHARMACOLOGICAL PROPERTIES

Vitamin D Calcium Supplement (medicinal product active on calcium checkup. A: digestive tract and metabolism).

5.1 Pharmacodynamic properties

Vitamin D corrects an insufficient intake of vitamin D and increases intestinal absorption of calcium.

Calcium intake corrects a lack of calcium in the diet.

The commonly accepted requirement of calcium in the elderly is 1500 mg/day.

The optimal amount of vitamin D in the elderly is 500 - 1000 IU/day.

Vitamin D and calcium correct secondary senile hyperparathyroidism.

In a double blind placebo controlled study of 18 months, including 3270 women aged 84 ± 6 years with a low intake of calcium and living in nursing homes, had their diet supplemented with colecalciferol (800 UI/day) + Calcium (1.2 g/day). A significant decrease in PTH secretion has been observed.

After 18 months, results of the intend to treat analysis showed 80 hip fractures (5.7%) in the Calcium Vitamin D group and 110 hip fractures (7.9%) in the placebo group ($p = 0.004$). Therefore, in these study conditions, the treatment of 1387 women prevented 30 hip fractures. After 36 months of follow up, 137 women presented at least one hip fracture (11.6%) in the Calcium Vitamin D group ($n = 1176$) and 178 (15.8%) in the placebo group ($n = 1127$) ($p \leq 0.02$).

5.2 Pharmacokinetic properties

During dissolution the calcium salt contained in Cacit Vitamin D3 is transformed into calcium citrate.

Calcium citrate is well absorbed, approximately 30% to 40% of the ingested dose.

Calcium is eliminated in the urine and faeces and secreted in the sweat.

Vitamin D is absorbed in the intestine and transported by protein binding in the blood to the liver (first hydroxylation) then to the kidney (second hydroxylation).

The non-hydroxylated vitamin D is stored in reserve compartments such as adipose and muscle tissue. Its plasma half-life is several days; it is eliminated in the faeces and the urine.

5.3 Preclinical safety data

No remarkable findings.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid anhydrous
Malic acid
Gluconolactone
Maltodextrin
Sodium cyclamate
Saccharin sodium
Lemon flavouring (containing: Sorbitol, Mannitol, D-gluconolactone, Dextrin, Gum arabic, Lemon oil)
Rice starch
Potassium carbonate
α-Tocopherol
Soya-bean oil hydrogenated
Gelatin
Sucrose
Corn starch

Quantity of sodium per sachet: 5 mg or 0.22 mmol

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 25 °C.

6.5 Nature and contents of container

4 g sachets (paper/aluminium/polyethylene); boxes of 20, 28, 30, 46, 50, 56, 60 or 100 sachets and sample pack of 10 sachets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Procter & Gamble Pharmaceuticals UK Limited
Rusham Park
Whitehall Lane
Egham
TW20 9NW
Surrey
UK

8 MARKETING AUTHORISATION NUMBER

PA 0170/018/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25th September 1996

Date of last renewal: 11th February 2006

10 DATE OF REVISION OF THE TEXT

February 2006