1. Name of the medicinal product

UCGOD Calcium 600 + D3 400 Caplets

2. Qualitative and quantitative composition

Each Caplet contains

Calcium carbonate equivalent to 600mg of Calcium

Vitamin D as Colecalciferol…… 400iu

For full list of excipients see 6.1

3. Pharmaceutical form

Caplets

4. Clinical particulars

4.1 Therapeutic indications

As an adjunct to specific therapy for osteoporosis and in situations requiring therapeutic supplementation of malnutrition e.g. in pregnancy and established vitamin D dependent osteomalacia.

The prevention and treatment of calcium deficiency/vitamin D deficiency especially in the housebound and institutionalised elderly subjects. Deficiency of the active moieties is indicated by raised levels of PTH, lowered 25-hydroxy vitamin D and raised alkaline phosphatase levels which are associated with increased bone loss.

4.2 Posology and method of administration

Oral.

Adults and Elderly and children above 12 years of age:

2 Caplets per day, preferably one Caplets each morning and evening.

Children:

Not recommended for children under 12 years.

4.3 Contraindications

Absolute contra-indications are hypercalcaemia resulting for example from myeloma, bone metastases or other malignant bone disease, sarcoidosis; primary hyperparathyroidism and vitamin D overdosage. Severe renal failure. Hypersensitivity to any of the Caplets ingredients.

Relative contra-indications are osteoporosis due to prolonged immobilisation, renal stones, severe hypercalciuria.

UCGOD Calcium 600 + D3 400 Caplets contains a small quantity of soya oil and is therefore contraindicated in patients who are allergic to peanuts or soya.

4.4 Special warnings and precautions for use

Patients with mild to moderate renal failure or mild hypercalciuria should be supervised carefully including periodic checks of plasma calcium levels and urinary calcium excretion.

In patients with a history of renal stones urinary calcium excretion should be measured to exclude hypercalciuria.

With long-term treatment it is advisable to monitor serum and urinary calcium levels and kidney function, and reduce or stop treatment temporarily if urinary calcium exceeds 7.5mmol/24 hours (300mg/24 hours).

During concomitant treatment with other high-dose sources of vitamin D and/or medications affecting serum calcium levels or absorption, or nutrients containing calcium (see section 4.5), there is a risk of hypercalcaemia and milk-alkali syndrome (See section 4.9). In these patients, serum calcium levels and renal function should be monitored.

Caution is required in patients receiving treatment for cardiovascular disease (see Section 4.5 – thiazide diuretics and cardiac glycosides including digitalis).

UCGOD Calcium 600 + D3 400 Caplets should also be used with caution in other patients with increased risk of hypercalcaemia e.g. patients with sarcoidosis or those suffering from malignancies.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Each Caplets contains a small amount of sugar (about 1.7 mg per Caplets) and may be harmful to teeth if used for a prolonged period.

Allowances should be made for calcium and vitamin D supplements from other sources.

4.5 Interaction with other medicinal products and other forms of interaction

The risk of hypercalcaemia should be considered in patients taking thiazide diuretics since these drugs can reduce urinary calcium excretion. Hypercalcaemia must be avoided in digitalised patients.

Certain foods (e.g. those containing oxalic acid, phosphate or phytic acid) may reduce the absorption of calcium.

Concomitant treatment with phenytoin or barbiturates can decrease the effect of vitamin D because of metabolic activation. Concomitant use of glucocorticoids can decrease the effect of vitamin D.

The effects of digitalis and other cardiac glycosides may be accentuated with the oral administration of calcium combined with Vitamin D. Strict medical supervision is needed and, if necessary monitoring of ECG and calcium.

Calcium salts may reduce the absorption of thyroxine, bisphosphonates, sodium fluoride, quinolone or tetracycline antibiotics, zinc, strontium ranelate and iron. It is advisable to allow a minimum period of four hours before taking the calcium.

Concomitant treatment with orlistat may reduce absorption of vitamin D.

4.6 Pregnancy and lactation

During pregnancy and lactation treatment with UCGOD Calcium 600 + D3 400 Caplets should always be under the direction of a physician. During pregnancy and lactation, requirements for calcium and vitamin D are increased but in deciding on the required supplementation allowances should be made for availability of these agents from other

sources. If UCGOD Calcium 600 + D3 400 Caplets and iron supplements are both required to be administered to the patient, they should be taken at different times (see Section 4.5).

Overdoses of vitamin D have shown teratogenic effects in pregnant animals. However, there have been no studies on the use of this medicinal product in human pregnancy and lactation. In humans, long term hypercalcaemia can lead to physical and mental retardation, aortic stenosis and retinopathy in a new born child. Vitamin D and its metabolites pass into the breast milk.

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

Hypersensitivity reactions including pruritus, wheezing, urticaria, oropharyngeal swelling and angioedema have been reported in the post-marketing environment.

The use of calcium supplements has, rarely, given rise to mild gastro-intestinal disturbances, such as constipation, flatulence, nausea, gastric pain, diarrhoea. Following administration of vitamin D supplements occasional skin rash has been reported. Hypercalciuria, and in rare cases hypercalcaemia have been seen with long term treatment at high dosages.

4.9 Overdose

The most serious consequence of acute or chronic overdose is hypercalcaemia due to vitamin D toxicity. Symptoms may include nausea, vomiting, polyuria, anorexia, weakness, apathy, thirst and constipation. Chronic overdoses can lead to vascular and organ calcification as a result of hypercalcaemia. Treatment should consist of stopping all intake of calcium and vitamin D and rehydration.

Milk-alkali syndrome may occur in patients who ingest large amounts of calcium.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium, combinations with vitamin D and/or other drugs, ATC code: A12AX

Strong evidence that supplemental calcium and vitamin D_3 can reduce the incidence of hip and other non-vertebral fractures derives from an 18 month randomised placebo controlled study in 3270 healthy elderly women living in nursing homes or apartments for elderly people. A positive effect on bone mineral density was also observed.

In patients treated with 1200mg elemental calcium and 800IU vitamin D_3 daily, i.e. the same dose delivered by two Caplets of UCGOD Calcium 600 + D3 400 Caplets, the number of hip fractures was 43% lower ($p=0.043$) and the total number of non vertebral fractures was 32% lower than among those who received placebo. Proximal femur bone mineral density after 18 months of treatment increased 2.7% in the calcium/vitamin D_3 group and decreased 4.6% in the placebo group ($p < 0.001$). In the calcium/vitamin D_3 group, the mean serum PTH concentration decreased by 44% from baseline at 18 months and serum 25-hydroxy-vitamin D concentration had increased by 162% over baseline.

Analysis of the intention-to-treat results showed a decreased probability of both hip fractures ($p = 0.004$) and other fractures ($p < 0.001$) in the calcium/vitamin D_3 treatment group. Analysis of the other two populations (active treatment and those treated and followed for 18 months) revealed comparable results to the intention-to-treat analysis. The odds ratio for hip fractures among women in the placebo group compared with those in the calcium/vitamin D_3 group was 1.7 (95% CI 1.0 to 2.8) and that for other nonvertebral fractures was 1.4 (95% CI 1.4 to 2.1). In the placebo group, there was a marked increase in the incidence of hip fractures over time whereas the incidence in the calcium/vitamin D_3 group was stable.

Thus treatment reduced the age-related risk of fracture at 18 months ($p = 0.007$ for hip fractures and $p = 0.009$ for all non-vertebral fractures). At 3 years follow-up, the decrease in fracture risk was maintained in the calcium/vitamin D_3 group.

5.2 Pharmacokinetic properties

The pharmacokinetic profiles of calcium and its salts are well known. Calcium carbonate is converted to calcium chloride by gastric acid. Calcium is absorbed to the extent of about 15-25% from the gastro-intestinal tract while the remainder reverts to insoluble calcium carbonate and calcium stearate, and is excreted in the faeces.

The pharmacokinetics of vitamin D is also well known. Vitamin D is well absorbed from the gastro- intestinal tract in the presence of bile. It is hydroxylated in the liver to form 25-hydroxycholecalciferol and then undergoes further hydroxylation in the kidney to form the active metabolite 1, 25 dihydroxycholecalciferol (calcitriol). The metabolites circulate in the blood bound to a specific α - globin, Vitamin D and its metabolites are excreted mainly in the bile and faeces.

5.3 Preclinical safety data

Calcium carbonate and vitamin D are well known and widely used materials and have been used in clinical practice for many years. As such toxicity is only likely to occur in chronic overdosage where hypercalcaemia could result.

6. Pharmaceutical particulars

6.1 List of excipients

Maize starch,
Lactose
Magnesium stearate
Talcum powder
Aerosil
Sodium starch glycolate
Povidone K30

6.2 Incompatibilities

Not applicable, oral preparation.

6.3 Shelf life

24 months

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

White jar and green cap

6.6 Special precautions for disposal and other handling

No special conditions.

7. Marketing authorization holder

Distributed by

UCGOD Pharmaceutical Limited.

6, Oba T.T, Dada Avenue, Dental Bus Stop

Alonge Idi-Iroko Road, Ota Ogun State, Nigeria.

Manufactured by

Daily Sun Pharmaceutical Company Limited

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