For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory 8041871-8883

GEMITROL

(Calcitriol, Calcium Carbonate and Zinc Capsules)

COMPOSITION

Each soft gelatin capsule contains:

Calcitriol	0.25 mcg
Calcium Carbonate	500 mg
(equivalent to elemental Calcium 200 mg)	
Zinc (as Zinc Sulfate USP)	7.5 mg

Approved colours used in capsule shell

DOSAGE FORM

Capsules for oral use.

DESCRIPTION

This formulation combines calcitriol, calcium and zinc.

Calcitriol is the active from of vitamin D3 (cholecalciferol). It is produced in the kidney from the vitamin D metabolite 25-hydroxyvitamin D3 (calcifediol). Vitamin D is important for the absorption of calcium from the stomach and for the functioning of calcium in the body.

The known sites of action of calcitriol are intestine, bone, kidney and parathyroid gland. In bone, calcitriol in conjunction with parathyroid hormone stimulates resorption of calcium; and in the kidney, calcitriol increases the tubular reabsorption of calcium.

Calcium plays a critical role in the body. It is essential for normal functioning of nerves, cells, muscle and bone. Calcium prevents bone loss and is associated with a modest reduction in fracture risk. Calcium and vitamin D preparations are used to prevent or to treat calcium deficiency. A vitamin D resistant state may exist in uremic patients because of the failure of the kidney to adequately produce calcitriol.

Zinc is a nutritional supplement important for normal growth and tissue repair. Urinary elimination of zinc is increased in osteoporotic women. Zinc depletion is shown to diminish the response of oral calcitriol when administered orally. Supplementary zinc not only improves calcitriol response but also helps to arrest bone loss in old postmenopausal women.

INDICATIONS

- Management of hypocalcaemia in patients undergoing dialysis for chronic renal failure. It has been shown to significantly reduce elevated parathyroid hormone (PTH) levels. Reduction of PTH has been shown to result in an improvement in renal osteodystrophy
- Post-menopausal osteoporosis.
- Hypocalcaemia in hypoparathyrodism
- Parathyroidectomy
- Vitamin D dependent rickets
- Renal tubular osteocalcaemia
- Sporadic and oncogenic hypophasphatemic osteomalacia
- X-linked hypophosphatemic osteomalacia
- Osteomalacia in Malabsorption syndrome
- Hypocalcaemia and hypomagnesaemia after small bowel resection
- Osteoporosis in males
- Psoriasis

DOSAGE AND ADMINISTRATION

The optimal dose must be carefully determined for each patient. The recommended initial dose is one capsule of this combination daily. If a satisfactory response in the biochemical parameters and clinical manifestations of the disease state is not observed, the dose may be increased by an increment of 1-2 capsules at two to four week intervals. In patients undergoing dialysis, the dose may be increased by an increment of 1capsule at 4 to 8 week intervals. During this titration period, serum calcium and phosphorus levels should be obtained at least twice weekly and if hypercalcaemia is noted, the drug should be immediately discontinued until normocalcaemia ensues. In patients undergoing dialysis, phosphorus, magnesium and alkaline phosphatase should be determined periodically. Patients should be informed of the symptoms of hypercalcaemia

CONTRAINDICATIONS

This combination should not be given to patients with hypercalcaemia or evidence of vitamin D toxicity.

WARNINGS AND PRECAUTIONS

Since calcitriol is the most potent metabolite of vitamin D available, vitamin D and its derivatives should be withheld during treatment. In patients undergoing dialysis, who have high serum phosphorus levels, appropriate serum phosphate binders should be used.

Drug Interactions

- Concomitant us of magnesium containing antacids and calcitriol may lead to the development of hypermagnesaemia.
- This combination should be avoided in patients on digitalis because hypercalcaemia in such patients may precipitate cardiac arrhythmias
- Higher doses of calcitriol may be required in patients taking barbiturates or anticonvulsants.
- The effect of calcitriol may be counteracted by corticosteroids.
- Cholestyramine may impair intestinal absorption of calcitriol
- Concurrent use of calcium containing formulations may reduce the response of verapamil and other calcium channel blockers.
- Oestrogens may increase calcium absorption and calcium may prevent absorption of etidronate.
- Calcium carbonate may reduce absorption of fluoroquinolones and the effects of gallium may be antagonized.
- Concurrent use with phenytoin decreases the bioavailability of both phenytoin and calcium.
- Calcium may also decrease the absorption of tetracyclines.
- Bran products (including brown bread) and some foods (e.g. proteins, phytates, some minerals) may decrease zinc absorption.

Renal impairment

The elimination half-life of calcitriol increased by at least two fold in chronic renal failure and hemodialysis patients compared to healthy subjects.

Hepatic impairment

Controlled studies examining the influence of hepatic disease on calcitriol have not been conducted.

Pregnancy

Category C.

There are no adequate and well-controlled studies in pregnant women. This combination should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

Calcitriol may be excreted in human milk. A mother should not nurse while taking This combination.

Pediatric use

Safety and efficacy of this drug has not been established in children.

Geriatric use

The dose selection for an elderly patient should be cautious, usually starting at the lower end of the dose range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant disease or other drug therapy.

UNDESIRABLE EFFECTS

Adverse effects are in general similar to those encountered with excessive vitamin D intake.

The early symptoms of vitamin D intoxication associated with hypercalcaemia include weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain and metallic taste. Late signs include polyuria, polydipsia, anorexia, weight loss, nocturia, conjunctivitis (calcific), pancreatitis, photophobia, rhinorrhea, pruritus, hyperthermia, decreased libido, elevated BUN, albuminuria, hypercholesterolaemia, elevated SGOT and SGPT, ectopic calcification, hypertension, cardiac arrhythmias and rarely, overt psychosis.

OVERDOSAGE

Administration of this formulation to patients in excess of their requirements can cause hypercalcaemia, hypercalciuria and hyperphosphataemia. Overdosage of any form of vitamin D is dangerous. Progressive hypercalcaemia due to overdosage of this formulation may be so severe as to require emergency attention. Sometimes hypercalciuria can also occur. Chronic hypercalcaemia can lead to generalized vascular calcification, nephrocalcinosis and other soft tissue calcification. The serum calcium times phosphate product (Ca x P) should not be allowed to exceed 70. Radiographic evaluation of suspect anatomical regions may be useful in the early detection of this condition.

Excessive intake of zinc may lead to overdosage symptoms like nausea, severe vomiting, dehydration, restlessness and sideroblastic anaemia (secondary to zinc induced copper depletion).

General treatment of hypercalcaemia (greater than 1 mg/dl above the upper limit of normal range) consists of immediate discontinuation of therapy. Serum calcium levels should be determined daily until normocalcaemia (8.5 to 10.5 mg/dl) ensues. Hypercalcaemia usually resolves in two to seven days. When serum calcium levels have returned to within normal limits, drug may be reinstituted at a dose lower than the prior therapy. Serum calcium levels should be obtained at least twice weekly after all dosage changes. Persistent or markedly elevated serum calcium levels may be corrected by dialysis against a calcium free dialysate.

The treatment of acute accidental overdosage of the drug should consist of general supportive measures. Serial serum electrolyte determinations (especially calcium), rate of urinary calcium excretion and assessment of electrocardiographic abnormalities due to hypercalcaemia should be obtained.

Such monitoring is critical in patients receiving digitalis. Due to the pharmacological action of calcitriol lasting only 3-5 days, further measures are probably unnecessary. However, should persistent and markedly elevated serum calcium levels occur, there are a variety of therapeutic alternatives, which may be considered, depending on the patient's underlying condition. These include the use of drugs such as phosphates and corticosteroids as well as measures to induce an appropriate forced diuresis. The use of peritoneal dialysis against a calcium free dialysate has also been reported.

EXPIRY DATE

Do not use later than the date of expiry.

STORAGE

Store below 30^{o}C, Protected from light and moisture

PRESENTATION

GEMITROL (Calcitriol, Calcium Carbonate and Zinc Capsules) is available in Alu-PVC/PVDC blister 15 capsules. Such 10 blister strip are packed along with leaflet in one carton

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