Nefmax™-CT

Calcitriol 0.25 mcg Capsules

Maximize Prevention of SHPT Progression

Product Description:

Nefmax-CT: Each soft gelatin capsule contains Calcitriol IP 0.25 mcg

General Information:

Calcitriol or 1,25-dihydroxycholecalciferol (1,25-$(OH)_2$-D3) is the active form of vitamin D.It is formed primarily in the kidney by enzymatic hydroxylation of 25-hydroxycholecalciferol.

Calcitriol production is stimulated by low blood calcium levels and parathyroid hormone. It regulates calcium levels by increasing the absorption of calcium and phosphate from the gastrointestinal tract, increasing calcium and phosphate reabsorption in the kidneys and inhibiting the release of PTH. Calcitriol is also commonly used as a medication in the treatment of hypocalcemia and osteoporosis.

Indication & Usage:

Pre-Dialysis Patients:

- In the management of secondary hyperparathyroidism (SHPT)
- Mineral bone disease in patients with moderate to severe chronic renal failure

Dialysis Patients:

- Hypocalcaemia
- Mineral bone disease in patients undergoing chronic renal dialysis

Hypoparathyroidism Patients:

Calcitriol is also indicated in the management of hypocalcemia and its clinical manifestations in patients with postsurgical hypoparathyroidism, idiopathic hypoparathyroidism, and pseudohypoparathyroidism.

Dosage and Administration:

- **Dialysis Patients:**The recommended initial dose of calcitriol is 0.25 mcg/day. Dosage may be increased by 0.25 mcg/day at 4 to 8-week intervals.
- **Hypoparathyroidism:**The recommended initial dosage of calcitriol is 0.25 mcg/day.Doses may be increased at 2 to 4-week intervals
- **Pre-dialysis Patients:**The recommended initial dosage of calcitriol is 0.25 mcg/day in adults and paediatric patients 3 years of age and older. This dosage may be increased if necessary, to 0.5 mcg/day.
  For paediatric patients less than 3 years of age, the recommended initial dosage of calcitriol is 10to 15 ng/kg/day.

Mechanism of action:

Calcitriol is the most active known form of vitamin D3.

Vitamin D presence is mainly depending on dietary intake and/or exposure to the ultraviolet rays of the sun. In ultraviolet rays, the conversion of 7-dehydrocholesterol to vitamin D3 (cholecalciferol) takes place.

Cholecalciferol is get hydroxylated in liver by 25 hydroxylase enzymes to 25-hydroxy vitamin D3(25-OH-D3).This 25-hydroxy vitamin D3 is again hydroxylated in kidney by VitaminD3-1alphahydroxylase(alpha-OHase) enzyme to produce 1,25 dihydroxy cholecalciferol (1,25 (OH)2 D3) (calcitriol)

Pharmacokinetic:

Absorption: Calcitriol is rapidly absorbed from the intestine. Peak serumconcentrations were reached within 3 to 6 hours following oraladministration of single doses of 0.25 mcg to 1 mcg.

Distribution:
Calcitriol is approximately 99.9% bound in blood. Calcitriol and other vitamin D
metabolites are transported in blood, by an alpha-globulin vitamin D binding protein. There isevidence that maternal calcitriol may enter the fetal circulation.

Metabolism:

The first pathway involves 24-hydroxylase activity in the kidney; this enzyme is also present in many target tissues which possess the vitamin D receptor such as the intestine. The end product of this pathway is a side chain shortened metabolite, calcitroic acid. The second pathway involves the conversion of calcitriol via the stepwise hydroxylation of carbon-26 and carbon-23, and cyclization to yield ultimately 1a,25R$(OH)_2$-26,23S-lactone D3. The lactone appears to be the major metabolite circulating in humans.

Excretion

The elimination half-life of calcitriol in serum after single oral doses is about 5 to 8 hours. However, the pharmacological effect of a single dose of calcitriol lasts at least 4 days. Calcitriol is excreted in the bile and may undergo enterohepatic circulation

Use in Specific Population:

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

Nursing Mother: Calcitriol may be excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions from calcitriol in nursing infants, a mother should not nurse while taking calcitriol capsules.

Paediatric Use: Safety and effectiveness of calcitriol in paediatric patients undergoing dialysis have not been established. Dosing guidelines have not been established for paediatric patients under 1 year of age with hypoparathyroidism or for paediatric patients less than 6 years of age with pseudohypoparathyroidism

Contraindication: Calcitriol should not be given to patients with hypercalcemia or evidence of vitamin D toxicity

Warning & Precaution:

Overdosage of any form of vitamin D is dangerous.

Progressive hypercalcemia due to overdosage of vitamin D and its metabolites may be so severe as to require emergency attention.
Chronic hypercalcemia can lead to generalized vascular calcification, nephrocalcinosis and other soft-tissue calcification.

The serum calcium times phosphate(Ca x P) product should not be allowed to exceed 70 mg^2/dL^2

The administration of calcitriol to patients in excess of their daily requirements can cause hypercalcemia, hypercalciuria, and hyperphosphatemia.

Drug Interaction:

Cholestyramine: Cholestyramine has been reported to reduce intestinal absorption of fat-soluble vitamins; as such it may impair intestinal absorption of calcitriol
Phenytoin/Phenobarbital: The coadministration of phenytoin or phenobarbital will not affect plasma concentrations of calcitriol,but may reduce endogenous plasma levels of 25(OH)D3 by accelerating metabolism. Since blood level of calcitriol will be reduced, higher doses of calcitriol may be necessary if these drugs are administered simultaneously.
Thiazides: Thiazides are known to induce hypercalcemia by the reduction of calcium excretion in urine. Some reports have shown that the concomitant administration of thiazides with calcitriol causes hypercalcemia. Therefore, precaution shouldbe taken when coadministration is necessary.
Corticosteroids:A relationship of functional antagonism exists between vitamin D analogues, which promote calcium absorption,and corticosteroids, which inhibit calcium absorption.

Phosphate-Binding Agents: Since calcitriol also has an effect on phosphate transport in the intestine, kidneys and bones,the dosage of phosphate-binding agents must be adjusted in accordance with the serum phosphate concentration.

Adverse Reactions:

Adverse effects of calcitriol are similar to those occurring with excessive vitamin D intake. The early and late signs and symptoms of vitamin D intoxication associated with hypercalcemia include:

Early: Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain,bone pain and metallic taste.

Late: Polyuria, polydipsia, anorexia, weight loss, pruritus, hypercholesterolemia, elevated SGOT and SGPT, ectopic calcification, nephrocalcinosis, hypertension, cardiac arrhythmias