Prescribing Information

PrAG-Vitamin D

10,000IU Tablets

Vitamin D (Cholecalciferol) Tablets

Therapeutic Classification: Vitamin

Prepared by:
Angita Pharma Inc.
1310, rue Nobel
Boucherville, Quebec
J4B 5H3

Date Prepared:
May 06, 2020

Submission Control No : 238109

Table of Contents

PrAG-Vitamin D

10,000IU Tablets

Prescribing Information

CLINICAL PHARMACOLOGY

Vitamin D is a fat-soluble vitamin and has properties of both vitamins and minerals. The term Vitamin D collectively refers to a group of structurally similar chemicals and their metabolites, which includes alfacalcidol (1 α hydroxycholecalciferol), calcitriol (1,25-dihydroxychole-calciferol), cholecalciferol (Vitamin D3), dihydrotachysterol (DHT) and ergocalciferol (Vitamin D2). These agents have antirachitic properties.

The biologic activity of 40 l.U. Vitamin D equals that of 1 g of ergocalciferol or cholecalciferol.

Vitamin D is essential for the absorption and utilisation of calcium and phosphate and aids in the mobilization of bone calcium and maintenance of serum calcium concentrations.

Cholecalciferol (Vitamin D3) is synthesised in the skin on exposure to ultraviolet radiation. Cholecalciferol is also present in fish liver oils. Ergocalciferol (Vitamin D2) is produced by ultraviolet irradiation of a provitamin D sterol (ergosterol) which occurs in yeast and fungi.

Both of these agents who have equal biologic activity are metabolised in the liver to calcifediol (25 hydroxycholecalciferol) which is then hydroxylated in the kidney to calcitriol (1,25 dihydroxycholecalciferol). Calcitriol is considered the most active form. Dihydrotachysterol is produced by synthetic reduction of ergocalciferol. Patients with chronic renal disease cannot convert calcifediol to calcitriol. Alfacalcidol (1 α hydroxyvitamin D3), a synthetic analogue of calcitriol, is rapidly converted in the liver to calcitriol, bypassing the renal conversion step.

Because alfacalcidol, calcitriol and dihydrotachysterol do not require renal hydroxylation, they are useful in patients with renal failure.

PHARMACOKINETICS

See Table 1.

Vitamin D analogues are readily absorbed from the small intestine if fat absorption is normal. Bile is required for absorption.

The 2 step process described above activates cholecalciferol and ergocalciferol. The liver activates Dihydrotachysterol and atfacalcidol. Vitamin D is eliminated renally and by biliary excretion.

Table 1.

	T ½ (Hours)	Onset of Action (Hours)	Duration of Action
Alfacalcidol	3	6	Up to 48 hours
Calcitriol	3 – 6	2 – 6	3 – 5 days
Dihydrotachysterol	N/A	Several	Up to 9 weeks
Ergocalciferol	19 – 48	12 – 24	Up to 6 months

INDICATIONS AND USAGE

Vitamin D analogues are used in treatment of refractory rickets (Vitamin D-resistant rickets), familial hypophosphatemia and hypoparathyroidism, and in the management of hypocalcemia and renal osteodystrophy in patients with chronic renal failure undergoing dialysis. Vitamin D is used in conjunction with calcium in the management and prevention of primary or corticosteroid-induced osteoporosis. Vitamin D supplementation is indicated when dietary intake is insufficient, e.g., breast-fed infants.

CONTRAINDICATIONS

Known hypersensitivity to Vitamin D or any of its analogues and derivatives. Hypercalcemia, malabsorption syndrome, abnormal sensitivity to the toxic effects of Vitamin D and hypervitaminosis D.

PRECAUTIONS

Vitamin D analogues are usually non-toxic in physiologic doses. Chronic or acute administration of excessive doses may lead to hypervitaminosis D, manifested by hypercalcemia and its sequelae.
The therapeutic index of Vitamin D analogues is narrow, and there is great interindividual variation in the dose that will lead be chronic toxicity. Daily doses of ergocalciferol ranging from 1.25 to 2.5 mg in adults and 25 µg in children may result in hypervitaminosis. Other Vitamin D analogues with shorter duration of action may have a lower propensity to accumulate and to cause hypercalcemia.

Early symptoms of hypercalcemia may include weakness, fatigue, somnolence, headache, anorexia, dry mouth, metallic taste, nausea, vomiting, vertigo, tinnitus, ataxia, hypotonia. Later and possibly more serious manifestations include nephrocalcinosis, renal dysfunction, osteoporosis in adults, impaired growth in children, anaemia, metastatic calcification, pancreatitis, generalised vascular calcification and seizures.

Periodic monitoring of serum calcium, phosphate, magnesium, alkaline phosphatase is recommended for patients taking Vitamin D analogues. Serum calcium should be maintained the range of 2.25 to 2.5 mmol/L and not allowed to exceed 2.75 mmol/L.

Drug Interactions

- Antacids (Magnesium-containing): Hypermagnesemia may develop when these agents are used concurrently with Vitamin D, particularly in patients with chronic renal failure.

- Anticonvulsants (Phenytoin, Phenobarbital): Decreased Vitamin D effects may occur when certain anticonvulsants are administered, as they may induce hepatic microsomial enzymes and accelerate the conversion of Vitamin D to inactive metabolites.

- Cholestyramine. Colestipol, Mineral OiI: Intestinal absorption of Vitamin D may be impaired. Patients on chotestyramine or colestipol should be advised to allow as much time as possible between the ingestion of these drugs and Vitamin D.

- Digoxin: Vitamin D should be used with caution in patients on digoxin as hypercalcemia (which may result with Vitamin D use) may precipitate cardiac arrhythmias.

- Thiazide Diuretics: Concurrent administration of thiazide diuretics and Vitamin D for hypoparathyroid patients may cause hypercalcemia, which may be transient or may require discontinuation of Vitamin D.

  Different Vitamin D analogues should be administered concurrently.

Use in Pregnancy

Safety of doses in excess of 400 l.U. (10 µg) of Vitamin D daily during pregnancy has not been established. Maternal hypercalcemia, possibly caused by excessive Vitamin D intake during pregnancy, has been associated with hypercalcemia in neonates, which may lead to supravalvular aortic stenosis syndrome, the features of which may include retinopathy, mental or growth retardation, strabismus and other effects.

Hypercalcemia during pregnancy may also lead to suppression of parathyroid hormone release in the neonate, resulting in hypocalcemia, tetany and seizures.

Lactation

Vitamin D is deficient in maternal milk; therefore breastfed infants may require supplementation. Use of excessive amounts of Vitamin D in nursing mothers may result in hypercalcemia in infants. Doses of Vitamin D analogues in excess of 10 µg daily should not be administered to nursing women.

ADVERSE REACTIONS

Vitamin D analogues are well tolerated in normal daily doses. Chronic excessive dosing can lead to toxicity (see Precautions).

OVERDOSAGE

Symptoms: Acute intoxication with Vitamin D analogues may cause hypervitaminosis D (See Precautions).

Treatment: Treatment of acute or chronic intoxication includes withdrawal of the Vitamin D analogues and any calcium supplements, administration of oral or IV. fluids and possibly corticosteroids or calciuric diuretics such as furosemide and ethacrynic acid. Peritoneal or hemodialysis with calcium free dialysate will help remove calcium.

If acute ingestion is recent, gastric lavage or emesis may minimise further absorption. If the drug has already passed through the stomach, administration of mineral oil may promote faecal elimination.

Hypercalcemia is usually reversible; however if metastatic calcification has occurred, severe renal or cardiac failure or even death may result.

DOSAGE AND ADMINISTRATION

In preventing Vitamin deficiencies, adequate dietary intake is preferred over supplementation whenever possible.

It should be noted that expert groups are now recommending daily intake of 400 to 1000 I.U of Vitamin D to optimise calcium absorption and prevent primary or corticosteroid-induced osteoporosis. Daily doses of 400 to 800 I.U and sometimes higher is used in conjunct with calcium and other measures in the treatment of osteoporosis.

At doses used for active treatment of deficiency, the range between therapeutic and toxic doses is narrow.

Dosage of Vitamin D analogues must be individualized with careful monitoring of serum calcium levels. Careful titration is necessary to avoid overdose. Dietary and other sources of vitamin D must be considered. Calcium intake should be adequate.

For Vitamin D deficiency, 5000 I.U. (125 μg) daily until a biochemical and radiographic response is achieved.

For Vitamin D-resistant rickets, 12 000 to 500 000 l.U. (0.3 to 12.5 mg) daily.

For hypoparathyroidism, 50 000 to 200 000 I.U. (1.25 to 5 mg) daily. Calcium supplementation is also required.

STORAGE AND STABILITY

Store in a cool, dry place.

DOSAGE FORMS, PACKAGING AND COMPOSITION

[Pr]AG-Vitamin D: White film-coated, round, biconvex tablets.

Available in bottles of 60 tablets.

Composition:

PrAG-Vitamin D contains Vitamin D3 (Cholecalciferol) 10 000 I.U.

Non-medicinal ingredients: Dibasic calcium phosphate dehydrate, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, talc, Opadry II White (hypromellose, titanium dioxide, talc, polydextrose, maltodextrin, medium chain triglycerides).