Size : 180 x 120 mm (Front)

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

Alfacalcidol Capsules

Panacea Biotec

Alphadol

COMPOSITION
Alphadol
Each soft gelatin capsule contains:
Alfacalcidol IP 0.25 mcg
Colour: Ponceau 4R Supra
Alphadol-0.5
Each soft gelatin capsule contains:
Alfacalcidol IP 0.5 mcg
Colour: Quinoline Yellow WS
Alphadol-1
Each soft gelatin capsule contains:
Alfacalcidol IP 1 mcg
Approved colours used in capsule shells
DOSAGE FORM/S
Capsules
INDICATIONS
Alfacalcidol is used for treating conditions in which calcium metabolism is disturbed due to impaired 1α-hydroxylation such as reduced renal function; osteoporosis associated with Vitamin D resistance and calcium malabsorption.
The main indications are:
Osteoporosis
Renal bone disease (renal osteodystrophy)
Hypoparathyroidism
Hyperparathyroidism (with bone disease)
Rickets and osteomalacia
DOSE AND METHOD OF ADMINISTRATION
Route of administration: oral
The capsules should be swallowed whole with a drink of water.
Initial dose for all indications excepting Osteoporosis
Adults: 1 microgram/day
Dosage in the elderly: 0.5 microgram/day
Children over 20kg bodyweight: 1 microgram/day
The dose of Alfacalcidol should be adjusted thereafter to avoid hypercalcaemia according to the biochemical response. Indices of response include plasma levels of calcium (ideally corrected for protein binding), alkaline phosphatase, parathyroid hormone, as well as radiographic and histological investigations.
Plasma levels should initially be measured at weekly intervals. The daily dose of Alfacalcidol may be increased by increments of 0.25 – 0.5 microgram. When the dose is stabilised, measurements may be taken every 2 – 4 weeks.
Most adult patients respond to doses between 1 and 3 micrograms per day. When there is biochemical or radiographic evidence of bone healing, (and in hypoparathyroid patients when normal plasma calcium levels have been attained), the dose generally decreases. Maintenance doses are generally in the range of 0.25 to 1 microgram per day. If hypercalcaemia occurs, Alfacalcidol should be stopped until plasma calcium returns to normal (approximately 1 week) then restarted at half the previous dose.
Renal bone disease
Patients with relatively high initial plasma calcium levels may have autonomous hyperparathyroidism, often unresponsive to Alfacalcidol. Other therapeutic measures may be indicated.
Before and during treatment with Alfacalcidol, phosphate binding agents should be considered to prevent hyperphosphataemia. It is particularly important to make frequent plasma calcium measurements in patients with chronic renal failure because prolonged hypercalcaemia may aggravate the decline of renal function.
Hyperparathyroidism
In patients with primary or tertiary hyperparathyroidism about to undergo parathyroidectomy, preoperative treatment with Alfacalcidol for 2-3 weeks alleviates bone pain and myopathy without aggravating pre-operative hypercalcaemia. In order to decrease post-operative hypocalcaemia, Alfacalcidol should be continued until plasma alkaline phosphatase levels fall to normal or hypercalcaemia occurs.
Hypoparathyroidism
In contrast to the response to parent vitamin D, low plasma calcium levels are restored to normal relatively quickly with Alfacalcidol. Severe hypocalcaemia is corrected more rapidly with higher doses of Alfacalcidol (e.g. 3-5 micrograms) together with calcium supplements.
Nutritional and malabsorptive rickets and osteomalacia
Nutritional rickets and osteomalacia can be cured rapidly with Alfacalcidol. Malabsorptive osteomalacia (responding to large doses of IM or IV parent vitamin D) will respond to small doses of Alfacalcidol.
Pseudo-deficiency (D-dependent) rickets and osteomalacia
Although large doses of parent vitamin D would be required, effective doses of Alfacalcidol are similar to those required to heal nutritional vitamin D deficiency rickets and osteomalacia.
Hypophosphataemic vitamin D-resistant rickets and osteomalacia
Neither large doses of parent vitamin D nor phosphate supplements are entirely satisfactory. Treatment with Alfacalcidol at normal dosage rapidly relieves myopathy when present and increases calcium and phosphate retention. Phosphate supplements may also be required in some patients.
Osteoporosis
The exact dosage in osteoporosis is not defined, however the various clinical studies have used the dosage in range of 0.5 -1 mcg/day with or without calcium in treatment of osteoporosis.
USE IN SPECIAL POPULATIONS
Pregnancy and lactation
There are no adequate data from the use of alfacalcidol in pregnant women. Animal studies are insufficient with respect to effects on pregnancy. The potential risks for humans are unknown. Caution should be taken when prescribing to pregnant women as hypercalcaemia during pregnancy may produce congenital disorders in the offspring.
Although it has not been established, it is likely that increased amounts of 1,25-dihydroxyvitamin D will be found in the milk of lactating mothers treated with alfacalcidol. This may influence calcium metabolism in the infant.
Use in Elderly
The clinical manifestations of hypo- or hyper calcaemia should be considered especially in elderly patients with pre-existing renal or heart conditions.
Paediatric population
Alfacalcidol should be used with caution in infants, who may have increased sensitivity to its effects.
Take care to ensure correct dose in infants.
CONTRA-INDICATIONS
Alphadol should not be administered in the presence of
- Hypersensitivity to alfacalcidol or any of the other ingredients
- Hypercalcemia
- Metastatic calcification
- Hyperphosphataemia (except when occurring with hypoparathyroidism)
- Hypermagnesaemia

WARNINGS & PRECAUTIONS
Alfacalcidol should be used with caution for:
- patients being treated with cardioactive glycosides or digitalis as hypercalcaemia may lead to

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arrhythmia in such patients
- patients with nephrolithiasis

During treatment with alfacalcidol, serum calcium and serum phosphate should be monitored regularly especially in children, patients with renal impairment and patients receiving high doses. To maintain serum phosphate at an acceptable level in patients with renal bone disease a phosphate binding agent may be used.
Hypercalcaemia may appear in patients treated with alfacalcidol, the early symptoms are as follows:
- Polyuria
- Polydipsia
- Weakness, headache, nausea, constipation
- Dry mouth
- Muscle and bone pain
- Metallic taste

Hypercalcaemia can be rapidly corrected by stopping treatment until plasma calcium levels return to normal (in about one week). Alfacalcidol treatment may then be restarted at a reduced dose (half the previous dose).
The dose of alfacalcidol should be adjusted to avoid hypercalcemia, according to the biochemical response. Indices of response, in addition to a rise in plasma calcium, may include a progressive reduction in alkaline phosphatase, a reduction in parathyroid hormone levels, an increase in urinary calcium excretion in patients with normal renal function, bone radiography and histological improvements
DRUG INTERACTIONS
Patients taking barbiturates or anticonvulsants may require larger doses of Alfacalcidol to produce the desired effect to the induction of hepatic detoxification enzymes.
Concomitant administration of colestyramine may interfere with the intestinal absorption of alfacalcidol.
Use with caution in patients being treated with thiazide diuretics as they may have an increased risk of developing hypercalcaemia.
Paediatric population
Drug interactions with Alfacalcidol are known to be similar in the paediatric age group and that in adults.
UNDESIRABLE EFFECTS
The most frequently reported undesirable effects are hypercalcaemia and various skin reactions.
Metabolism and Nutrition Disorders : Hypercalcaemia ,Hyperphosphataemia
Skin and Subcutaneous Tissue Disorders : Pruritus, Rash, Urticaria
Renal and Urinary Disorders : Nephrocalcinosis ,Renal impairment
Paediatric population : Frequency and type of adverse reactions in children are the same as in adults.
OVERDOSE
Hypercalcaemia is treated by stopping Alfacalcidol.
In severe cases of hypercalcaemia general supportive measures should be undertaken. Keep the patient well hydrated by i.v. infusion of saline (force diuresis), measure electrolytes, calcium and renal function indices; assess electrocardiographic abnormalities, especially in patients on digitalis. More specifically, treatment with glucocorticosteroids, loop diuretics, bisphosphonates, calcitonin and eventually haemodialysis with low calcium content should be considered.
Paediatric population
Infants and children are generally more susceptible to the toxic effects of vitamin D.
PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: Vitamin D and analogues.
ATC code:A11CC03
Alfacalcidol is converted rapidly in the liver to 1, 25-dihydroxyvitamin D. This is the metabolite of vitamin D which acts as a regulator of calcium and phosphate metabolism. Since this conversion is rapid, the clinical effects of Alfacalcidol and 1, 25-dihydroxyvitamin D are very similar.
Impaired 1-α hydroxylation by the kidneys reduces endogenous 1,25-dihydroxyvitamin D production. This contributes to the disturbances in mineral metabolism found in several disorders, including renal bone disease and hypoparathyoidism. These disorders, which require high doses of parent vitamin D for their correction, will respond to small doses of Alfacalcidol.
The delay in response and high dosage required in treating these disorders with parent vitamin D makes dosage adjustment difficult. This can result in unpredictable hypercalcaemia which may take weeks or months to reverse. The major advantage of Alfacalcidol is the more rapid onset of response, which allows a more accurate titration of dosage. Should inadvertent hypercalcaemia occur it can be reversed within days of stopping treatment.
Paediatric population
When 1-α hydroxylation by the kidneys is impaired, endogenous 1,25-dihydroxyvitamin D production is reduced. Disorders in which this can occur include neonatal hypocalcaemia and Vitamin D-dependent rickets. Such conditions require high doses of Vitamin D for their correction but will respond to small doses of Alfacalcidol, which does not depend on the renal 1-α hydroxylation process.
Pharmacokinetic Properties
Absorption
In patients with renal failure, 1-5 µg/day of 1α - hydroxyvitamin D (1α-OHD3) increased intestinal calcium and phosphorus absorption in a dose-related manner. This effect was observed within 3 days of starting the drug and conversely, it was reversed within 3 days of its discontinuation.
In patients with nutritional osteomalacia, increases in calcium absorption were noted within 6 hours of giving 1 µg 1α-OHD3 orally and usually peaked at 24 hours. 1α-OHD3 also produced increases in plasma inorganic phosphorus due to increased intestinal absorption and renal tubular re-absorption. This latter effect is a result of PTH suppression by 1α-OHD3. The effect of the drug on calcium was about double its effect on phosphorus absorption.
Patients with chronic renal failure have shown increased serum calcium levels within 5 days of receiving 1α-OHD3 in a dose of 0.5 - 1.0 µg/day. As serum calcium rose, PTH levels and alkaline phosphatase decreased toward normal.
Distribution
Vitamin D and its metabolites circulate in the blood bound to a specific α-globulin. Alfacalcidol has a more rapid action and shorter half-life.
Biotransformation
Alfacalcidol undergoes rapid hepatic conversion to 1,25-dihydroxyvitamin D, the Vitamin D metabolite which acts as a regulator of calcium and phosphate metabolism.
Elimination
Vitamin D compounds and their metabolites are excreted mainly in the bile and faeces with only small amounts appearing in urine; there is some enterohepatic recycling but it is considered to have a negligible contribution to vitamin D status.
Paediatric population
Limited data is available in children.
INCOMPATIBILITIES
Not applicable
SHELF-LIFE
For shelf life refer the outer Carton.
PACKAGING INFORMATION
Alphadol: Available in box of blister strip of 10 X 10's.
Alphadol 0.5: Available in box of blister strip of 10 X 10's.
Alphadol-1: Available in box of blister strip of 3 X 10's.
STORAGE AND HANDLING INSTRUCTIONS
Store at a temperature below 25°C, protect from light and moisture.

For more information and details contact :
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PPIA033E

Product Name	**Alphadol**		**Change Control No.: BCC293/17**
Item Code	PPIA033E	**Colours:**	Black
Size	180x120 mm		
Market	Domestic		
		Revision No: 00	