

Alfaget™

(ALFACALCIDOL TABLETS 0.5mcg)

Tablets

DESCRIPTION

ALFAGET (Alfacalcidol) is a Vitamin-D analogue which acts as calcium and phosphate regulator. Chemically, alfacalcidol is described as (5Z, 7E),-9,10-secocholesta-5,7,10 (19)-triene-1 α ,3 β -diol. The molecular formula is C₂₇H₄₄O₂ and the structural formula is:



QUALITATIVE & QUANTITATIVE COMPOSITION

ALFAGET (Alfacalcidol) 0.5mcg is available as tablets for oral administration.

Each tablet contains:
Alfacalcidol BP...0.5mcg

CLINICAL PHARMACOLOGY

Mechanism of Action

Alfacalcidol is a Vitamin-D analogue. It acts as a regulator of calcium and phosphate metabolism. Its active metabolite 1,25-dihydroxyvitamin D₃ binds to receptors distributed in the target tissues, the intestine and bones, where it expresses a series of physiological activities, including promoting calcium absorption from the intestine, bone mineral dissolution, and osteogenic activity.

Pharmacokinetics

Following oral administration, alfacalcidol is rapidly absorbed into blood through intestine and the 25-position of the side chain is hydroxylated, with 25-hydroxylase of hepatic microsome, into the final active substance, in the liver, into 1 α , 25(OH)2D₃. It binds with receptors in intestinal tract, bone and other target organs and develops series of physiological activities, such as promotion of calcium absorption from intestine, bone resorption and bone formation activities. The peak level is observed at 8-24 hours after the administration and the half life is 2-4 days in normal adults with oral administration of alfacalcidol 4mcg/day. Alfacalcidol circulates in the blood, bound to specific alpha globulins and is stored in adipose and muscle tissue for long periods of time. Approximately 72% of an oral dose of alfacalcidol is excreted in the urine and feces within 48 hours and almost 100% excreted in 7 days. The biological half-life is approximately 35 hours.

The presence of bile is essential for adequate intestinal absorption; absorption may be decreased in patients with decreased fat absorption.

THERAPEUTIC INDICATIONS

ALFAGET (Alfacalcidol) is used for treating conditions in which calcium metabolism is disturbed due to impaired 1 α -hydroxylation, such as reduced renal function and in other disorders associated with Vitamin D resistance.

ALFAGET (Alfacalcidol) is indicated for:

- Renal bone disease (Renal Osteodystrophy).
- Hypoparathyroidism (e.g. Postoperative or Idiopathic Hypoparathyroidism, Pseudohypoparathyroidism).

- Hyperparathyroidism (with bone disease).
- Nutritional and malabsorptive rickets and osteomalacia.
- Neonatal hypocalcaemia.
- Hypophosphatemic Vitamin D-resistant rickets and osteomalacia.
- Pseudo-deficiency (D-dependent Type I) rickets and osteomalacia.
- Malabsorption of calcium.
- Primary and secondary osteoporosis; osteopenia.

DOSAGE AND ADMINISTRATION

For all indications except osteoporosis:

Adults	1mcg/day
Elderly patients	0.5mcg/day
Children under 20Kg	0.05mcg/day
Children 20Kg and over except in renal osteodystrophy	1mcg/day

The dose of ALFAGET (Alfacalcidol) should be adjusted thereafter to avoid hypercalcemia. Plasma levels should initially be measured at weekly intervals. The daily dose of ALFAGET (Alfacalcidol) may be increased by increments of 0.5mcg. When the dose is stabilised, measurements may be taken every 2-4 weeks.

Most adults respond to doses of 1-3mcg/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 dose:

The dose required for maintenance are generally in the range of 0.25 to 1mcg/day. Should hypercalcemia occur, ALFAGET (Alfacalcidol) should be stopped until plasma calcium returns to normal (usually about a week) then restarted at one half of the previous dose.

Osteoporosis:

The usual dose of ALFAGET (Alfacalcidol) is 0.5mcg/day in adults. The recommended maintenance dose is 0.5-1mcg/day which should not be exceeded. The general oral dose for children with osteoporosis ranges 0.01-0.03mcg/kg once a day.

Renal Bone Disease (Renal Osteodystrophy):

The dose for children 20kg and over with renal osteodystrophy is 0.04-0.08mcg/kg/day. Children seem to need relatively higher dose than adults and may even need the adult dose.

Hypoparathyroidism/Hyperparathyroidism:

For adults 1-4mcg of ALFAGET (Alfacalcidol) is given orally once a day. Severe hypocalcemia is corrected more rapidly with higher doses of ALFAGET (Alfacalcidol) e.g. 3-5mcg, together with calcium supplements.

ALFAGET (Alfacalcidol) can be given for 2-3 weeks as pre-operative treatment for primary or tertiary hyperparathyroidism surgery.

ADVERSE REACTIONS

No side effects associated directly with alfacalcidol therapy have been noted.

CONTRAINDICATIONS

- Alfacalcidol should not be used in patients with evidence of Vitamin D toxicity or known hypersensitivity to the effects of Vitamin D or any of its analogues.
- Alfacalcidol should not be administered in the presence of hypercalcemia, hyperphosphatemia (except when occurring with hypoparathyroidism) or hypermagnesemia

PRECAUTIONS

Monitoring of calcium, phosphate, alkaline phosphatase, magnesium and creatinine levels as well as other appropriate biochemical parameters should be done regularly.

Use in the Elderly

Attention to the dose should be required due to generally lower physiologic functions.

Pediatric use

Administration to children should be made with caution to avoid overdose, by gradual dose increase after an initial lower dose under the monitoring of serum calcium level, urinary calcium level and urinary calcium creatinine ratio.

Pregnancy and Nursing Mothers

There are no adequate and well-controlled studies in pregnant and nursing women. Alfacalcidol should be used only if the potential benefit justifies the potential risk to the fetus and infant.

Drug Interactions

Digitalis glycosides:

Hypercalcemia in patients taking digitalis preparations may precipitate cardiac arrhythmias. Patients taking digitalis concurrently with alfacalcidol must therefore be closely monitored.

Magnesium:

Caution should be exercised in the use of magnesium based antacids or laxatives for patients taking alfacalcidol who are on chronic renal dialysis. Hypermagnesemia may occur.

OVERDOSAGE

In the event of overdose, alfacalcidol should immediately be stopped and in severe hypercalcemia additional treatment with loop diuretics and intravenous fluids, or corticosteroids is done.

STORAGE

Store below 30°C.

Protect from sunlight and moisture.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED

ALFAGET (Alfacalcidol) tablets 0.5mcg are available in blister pack of 10's.

Keep out of reach of children.

To be sold on prescription of a registered medical practitioner only.

Please read the contents carefully before use.
This package insert is continually updated from time to time.



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