United Pharmaceuticals

OSTEO-ALFA 0.25 & 1.0 µg Soft gelatin capsules

Alfacalcidol

Name of product:
OSTEO-ALFA Soft gelatin capsule 0.25 µg
OSTEO-ALFA Soft gelatin capsule 1.0 µg

Name and strength of active ingredient:
Alfacalcidol 0.25 µg
Alfacalcidol 1.0 µg

Product description:
OSTEO-ALFA (Alfacalcidol) 0.25 µg - Oval reddish brown soft gelatin capsules contains clear, transparent yellow oily liquid.

OSTEO-ALFA (Alfacalcidol) 1.0 µg - Oval dark brown soft gelatin capsules contains clear, transparent yellow oily liquid.

Pharmacodynamic:
• **OSTEO-ALFA** which contains 'Alfacalcidol (1-alpha-hydroxyvitamin D3)' 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-alfa 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, hypoparathyroidism, neonatal hypocalcaemia and vitamin D dependent rickets. 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.

Pharmacokinetics:
• Alfacalcidol is well absorbed from gastrointestinal tract, and mainly excreted in the bile and faces.
• In patients with renal failure, 1-5 ug/day of 1 α-hydroxyvitamin D (1 α-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 ug 1 α-OHD3 orally and usually peaks at 24 hours. 1 α-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 1 α-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 level within 5 days of receiving 1 α-OHD3 in a dose of 0.5 – 1.0 ug/day. As serum calcium rose, PTH levels and alkaline phosphatase decreased toward normal.
• ADME:
- *Absorption:*
Alfacalcidol appears well-absorbed after oral doses.
- *Metabolism:*
Alfacalcidol undergoes hepatic 25-hydroxylation to 1,25 dihydroxycholecalciferol (calcitriol) following oral or intravenous administration. This occurs rapidly (ie, 2 hours) with resultant acute rises in plasma calcitriol levels.
- *Excretion:*
Alfacalcidol is excreted mainly in the bile and faces with only small amounts appearing in urine.
- *Elimination half-life:*
Approximately 3 hours

Indications:
OSTEO-ALFA is indicated in:
• Disease caused by disturbances in calcium metabolism in consequence of reduced endogenous production of 1,25-dihydroxyvitamin D3 due to impaired kidney functions, renal osteodystrophy.
• Vitamin D deficiency which develops when there is inadequate exposure to sunlight, or lack of Vitamin D in diet and in persons with fat malabsorption syndromes. Deficiency leads to development of hypocalcaemia, hypophosphatemia and bone demineralization, bone fracture, and muscle weakness known in adults as osteomalacia and in children as rickets.
• Postmenopausal osteoporosis, hypoparathyroidism, and adjunct to hyperparathyroidism management.

Recommended Dose:
Adult and children with 20 kg body weight or above: 0.5 - 1 µg/day.

Adult and children with less than 20 kg body weight: 0.05 µg/kg/day.

Neonates: 0.1 µg/kg/day.

It is important to adjust the dosage according to the biochemical responses to avoid hypercalcaemia. Monitor levels of serum calcium, alkaline phosphatase, parathyroid hormone, urinary calcium excretion as well as radiographic and histological investigations.

Apr., 2024
M3-14-1646

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Contraindication:
• Hypersensitivity to Vitamin D or its derivatives.
• Hypercalcaemia, hypercalciuria, hyperphosphatemia (except when occurring with hypoparathyroidism), hypermagnesaemia in those on chronic dialysis.

Warnings and Precautions
• Regular monitoring of serum calcium levels and serum alkaline phosphatase in monthly intervals is essential.
• Alfacalcidol should be used with care in patients with renal failure, renal calculi or heart disease.
• In patients with renal bone disease, Alfacalcidol should be co-administered with phosphate binding agents to prevent hyperphosphatemia which can increase the risk of metastatic calcification.
• Preexisting cardiac conditions (potential exacerbation related to persistent hypercalcaemic effects during therapeutic use).
• Arteriosclerosis (potential exacerbation related to persistent hypercalcaemic effects during therapeutic use).
• Renal impairment (potential exacerbation related to persistent hypercalcaemic effects during therapeutic use).
• Liver disease (impaired absorption and hepatic 25-hydroxylation to calcitriol).
• Hyperphosphatemia (risk of metastatic calcification).
• Sarcoidosis/other granulomatous disease (potential for enhanced sensitivity to vitamin D).
• Concurrent use of calcium-containing preparations, other vitamin D-containing preparations or vitamin D analogues, or thiazide diuretics (enhanced risk of hypercalcaemia).
• Concurrent use of magnesium-containing antacids (potential for hypermagnesemia).
• Concurrent use of digitalis glycosides (potential for arrhythmias related to hypercalcaemic effects of Alfacalcidol).

Interactions with other medicaments:
• Digitalis Preparation: Cardiac arrhythmias precipitated.
• Thiazide Diuretics: Hypercalcaemic response enhanced.
• Barbiturates & other enzyme inducing anticonvulsants: Reduce efficacy
• Mineral Oil: Prolonged use reduces efficacy.
• Cholestyramine, Colestipol Sucralfate, Aluminum based Antacids: Reduce efficacy by decreasing absorption of Alfacalcidol.
• Magnesium based Antacids or Laxatives which inhibit gastrointestinal absorption of Vitamin D by binding to bile salts.

Pregnancy and Lactation:
Alfacalcidol should only be used in pregnancy and during lactation if considered essential by physician.

Side effects:
Hypercalcaemia and hyperphosphatemia

Symptoms and treatment overdose:
• Hypercalcaemia – associated with muscle weakness, headache, vertigo, lassitude, polyuria, sweating, diarrhea, anorexia, thirst, nausea and vomiting, - is treated by stopping Alfacalcidol treatment.
• Severe hypercalcaemia may require additional treatment with a “loop” diuretic intravenous fluids and corticosteroids.

Storage Conditions:
Store up to 30ºC.
Keep out of reach of children.
Jauhkan ubat daripada kanak-kanak.

Shelf life:
- **Osteo-Alfa** 0.25µg is 2 years.
- **Osteo-Alfa** 1.0µg is 3 years.

Pack size:
- 30 Soft gelatin capsules.
- 100 Soft gelatin capsules.

Manufactured by:
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MAL06121071X
MAL07082986X

Apr., 2024
M3-14-1646