Opt-D®

5mg/ml (200,000 IU) 1 Ampoule

Vitamin D_3 (Cholecalciferol)

Oral/IM Ampoule

آپٹ-ڈی

۵ ملی گرام / ملی لیٹر (۲۰۰،۰۰۰ آئی یو) ایمپیول

اورل / عضلاتی ایمپیول

COMPOSITION
Each ml Contains
Cholecalciferol (B.P).....5mg
(Innovator's Specs.)

DESCRIPTION
Opt-D Injection contains Cholecalciferol, a Vitamin D analogue also referred to as Vitamin D3. It is a fat soluble vitamin and is a precursor of the active hormone 1, 25-dihydroxy cholecalciferol, also known as Calcitriol. Chemically it is (3β, 5Z, 7E)-9, 10-secocholesta-5, 7, 10(19)-trien-3-ol and molecular formula is $C_{27}H_{44}O$.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Mechanism of Action
Cholecalciferol is produced within the skin under the influence of UV radiation including sunlight. In its biologically active form, cholecalciferol stimulates intestinal calcium absorption, incorporation of calcium into the osteoid, and release of calcium from bone tissue. In the small intestine it promotes rapid and delayed calcium uptake. The passive and active transport of phosphate is also stimulated. In the kidney, it inhibits the excretion of calcium and phosphate by promoting tubular resorption. The production of parathyroid hormone (PTH) in the parathyroids is inhibited directly by the biologically active form of cholecalciferol. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active cholecalciferol.

Pharmacokinetics

Absorption
Cholecalciferol from nutritional sources is almost completely absorbed from within the gastro-intestinal tract in the presence of dietary lipids and bile acids.

Distribution & Metabolism
Cholecalciferol is stored in fat cells. Cholecalciferol is metabolized by microsomal hydroxylase to form 25-hydroxycholecalciferol (25(OH) D_3, calcidiol), the primary storage form of vitamin D_3. 25(OH) D_3 undergoes a secondary hydroxylation within the kidney to form the predominant active metabolite 1, 25-hydroxycholecalciferol (1, 25$(OH)_2D_3$, calcitriol). The metabolites circulate in the blood bound to a specific α-globin.
After a single oral dose of cholecalciferol, the maximum serum concentrations of the primary storage form are reached after approximately 7 days.

Elimination
Cholecalciferol and its metabolites are excreted mainly in bile and faeces. 25(OH) D_3 is slowly eliminated with an apparent half-life in serum of about 50 days.

INDICATIONS
- Prevention and treatment of vitamin D deficiency.
- Building and keeping strong bones.
- Osteoporosis
- Disorders such as hypo-parathyroidism, pseudo-hypoparathyroidism, and familial hypophosphatemia.
- It may be used in kidney disease to keep calcium levels normal and allow normal bone growth.

DOSAGE AND ADMINISTRATION

Dose can be adjusted according to the severity of deficiency.
Opt-D (Cholecalciferol) Injection 5mg/mL can be administered orally or by IMroute in:
Infants receiving Vitamin D enriched milk:
0.5mL (100,000 IU) every 6 months
Nursed infants or infants not receiving Vitamin D enriched milk orchildren up to 5 years of age:
1mL (200,000 IU) every 6 months
Adolescents:1mL (200,000 IU) every 6 months during winter
Pregnant women:
0.5mL (100,000 IU) from the 6th or 7th month of pregnancy, repeated onceat the end of a month if the final trimester starts up in winter or in case ofnon solar exposure
Women after menopause:
1mL (200,000 IU) every year or every 6 months
Elderly:
0.5mL (100,000 IU) every 3 months
Digestive disorder:
0 .5mL to 1mL (100 ,000 - 200,000 IU) every 3 to 6 months
Patients receiving anticonvulsant treatment:
0.5 mL to 1mL (100,000-200, 000 IU) every 3 to 6 months
Vitamin D deficiency (Rickets, Osteomalacia, Hypocalcemia):
1mL (200,000 IU), can be repeated after 1 to 6 months

CONTRAINDICATIONS

Cholecalciferol must not be used in patients with:
- Hypersensitivity to the active substance (cholecalciferol) or any Vitamin D analogue
- Hypercalcaemia and/or hypercalciuria
- Nephrolithiasis (Renal calculi)
- Hypervitaminosis D
- Severe renal impairment
- Metastatic calcification
- William syndrome

WARNING AND PRECAUTIONS

Renal Impairment
Cholecalciferol should be used with caution in patients with impairment of renal function due to the potential exacerbation related to hypercalcemic effects during therapeutic use. The effect on calcium and phosphate levels should also be monitored. The risk of soft tissue calcification should be taken into account. In patients with severe renal insufficiency, vitamin D in the form of cholecalciferol is not metabolized normally and other forms of vitamin D should be used.

Hepatic Impairment
In patients with liver impairment, Vitamin D absorption may be markedly impaired; conversion to active metabolite calcifediol may be reduced significantly, with the requirement of high doses of cholecalciferol. Agents not requiring hepatic hydroxylation are preferred in this condition. It is not reasonable to use cholecalciferol in severe liver impairment.

Renal calculi
Cholecalciferol should not be taken by patients with a tendency to form calcium-containing renal calculi.

Cardiac disorders
Caution is required in patients receiving treatment for cardiovascular disease. There is a risk of potential exacerbation of cardiac disorders and arteriosclerosis related to persistent hypercalcemic effects during therapeutic use.

Sarcoidosis
Cholecalciferol should be prescribed with caution to patients suffering from sarcoidosis because of the risk of increased metabolism of vitamin D to its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Serum calcium monitoring
All patients receiving high, pharmacological doses of cholecalciferol and those with renal impairment should have their plasma calcium concentration monitored at intervals (initially once or twice weekly) and whenever nausea or vomiting occurs.

Calcium supplementation
Calcium supplementation should be considered for individual patients. Calcium supplements should be given under close medical supervision. Medical supervision is required whilst on treatment to prevent hypercalcaemia.

Risk of hypercalcemia due to concomitant medications
Concurrent use of calcium-containing preparations, other vitamin D-containing preparations or vitamin D analogs, or thiazide diuretics with cholecalciferol may predispose to (enhanced risk of hypercalcemia). See DRUG INTERACTIONS.

Hyperlipidemia
Cholecalciferol may cause a potential exacerbation of LDL elevation.

Hyperphosphatemia
There is a risk of metastatic calcification; normalization of phosphate levels is indicated prior to therapy with cholecaciferol.

Arteriosclerosis
There is a risk of potential exacerbation related to persistent hypercalcemic effects during therapeutic use

Effects on ability to drive and use machines
Cholecalciferol has no known side effects that are likely to affect the ability to drive and use or operate machines.

ADVERSE REACTIONS

Vitamin D3 (Cholcalciferol) is well-tolerated in therapeutic doses. Following adverse effects may occur however:

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia, Hypercalciuria
Skin and Subcutaneous disorders
Rare: Pruritus, Rash, Urticaria

Gastrointestinal disorders
Common: Constipation, Loss of appetite, Nausea
Adverse effects observed with over dosage of Cholecalciferol (Hypervitaminosis - D) are given in OVERDOSAGE section.

DRUG INTERACTIONS

• Patients co-treated with cardiac glycosides along with cholecalciferol may be susceptible to high calcium levels and should have ECG parameters and calcium levels monitored. It is recommended to reduce the dose or interrupt treatment if the calcium content in the urine exceeds 7.5 mmol/24 hours (300 mg/24 hours).
• Simultaneous administration of benzothiadiazine derivatives (thiazide diuretics) increases the risk of hypercalcaemia because they decrease the calcium excretion in the urine. The calcium levels in plasma and urine should therefore be monitored for patients undergoing long-term treatment.
• If cholecalciferol is combined with metabolites or analogues of vitamin D careful monitoring of serum calcium levels is recommended.
• Anti-convulsants e.g. phenytoin, phenobarbital, primidone, carbamazapine may diminish the effect of cholecalciferol due to hepatic enzyme induction.
• Rifampicin may reduce the effectiveness of cholecalciferol due to hepatic enzyme induction.
• Isoniazid may reduce the effectiveness of cholecalciferol due to inhibition of the metabolic activation of cholecalciferol.
• Drugs leading to fat malabsorption, e.g. orlistat, liquid paraffin, cholestyramine, may impair the absorption of cholecalciferol.
• The cytotoxic agent actinomycin and imidazole antifungal agents interfere with vitamin D activity by inhibiting the conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D by the kidney enzyme, 25-hydroxyvitamin D-1-hydroxylase.
• Concomitant use of glucocorticoids can decrease the effect of vitamin D.
• Concurrent use of CHOLECALCIFEROL and CIMETIDINE may result in decreased Systemic cholecalciferol (vitamin D) concentrations.
• Concurrent use of ANTACIDS and CHOLECALCIFEROL may result in aluminum toxicity.

USE IN SPECIAL POPULATIONS

Pregnancy
The recommended daily intake for pregnant women is 400 IU, however, in women who are considered to be vitamin D3 deficient a higher dose may be required (up to 2 000 IU/day – 5 drops). During pregnancy women should follow the advice of their medical practitioner as their requirements may vary depending on the severity of their disease and their response to treatment. Therapeutic doses of Cholecalciferol are unlikely to be harmful during pregnancy

Nursing mothers
Vitamin D3 can be prescribed while the patient is breast-feeding if necessary. This supplementation does not replace the administration of vitamin D3 in the neonate.
Overdose in infants induced by nursing mothers has not been observed; however, when prescribing additional vitamin D3 to a breast-fed child the practitioner should consider the dose of any additional vitamin D3 given to the mother.
Cholecalciferol and its metabolites are excreted in breast milk. Caution is required with high doses to prevent the potential risk of hypercalcemia in infants. Serum calciummonitoring is advised.

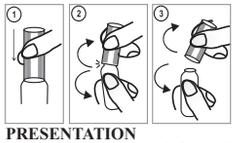
Renal Impairment
No dosage adjustment is needed in patients with renal impairment. Cholecalciferol should be used with caution in patients with impairment of renal function due to the potential exacerbation related to hypercalcemic effects during therapeutic use. Cholecalciferol must not be used in severe renal impairment metabolic as conversion to the active metabolite calcitriol is impaired and higher doses are generally required in most conditions. See WARNINGS AND PRECAUTIONS.

Hepatic Impairment
No dosage adjustment is needed. For details see WARNINGS AND PRECAUTIONS.

OVER DOSAGE
Symptoms
Acute or chronic overdose of Cholecalciferol can cause hypercalcaemia, an increase in the serum and urinary concentrations of calcium. The symptoms of hypercalcaemia are not very specific and consist of nausea, vomiting, diarrhoea often in the early stages and later constipation, anorexia, fatigue, headache, muscle and joint pain, muscle weakness, polydipsia, polyuria formation of renal calculi, nephrocalcinosis, kidney failure, and calcification of soft tissues, changes in ECG measurements, arrhythmias and pancreatitis. In rare and isolated cases there are reports that hypercalcaemia is fatal.

Treatment of overdose
A normalization of hypercalcaemia due to vitamin D intoxication lasts several weeks. The recommendation for the treatment of hypercalcaemia is the avoidance of any further administration of vitamin D, including supplements, dietary intakes and the avoidance of sunlight. A low calcium or calcium-free diet can also be considered. Monitoring of CNS and renal functioning should be done. Rehydration and the treatment with diuretics e.g. furosemide to ensure adequate diuresis should be considered. Additional treatment with calcitonin or corticosteroids can also be considered. Seizures should be treated with benzodiazepines followed by barbiturates as needed. Phosphate infusions should not be administered to lower hypercalcaemia of hypervitaminosis D because of the dangers of metastatic calcification.

AMPOULE BREAKING TECHNIQUE
- Hold the ampoule breaker & break the ampoule with slight thumb pressure.
- By this method ampoule will be broken safely and easily.



ایمپیول توڑنے کا آسان طریقہ
- ایمپیول (بینگ) کی ٹپ پر ایمپیول بریکر لگائیں۔
- ایمپیول بریکر پکڑ کر باہر کی طرف انگوٹھے کی مدد سے ہلکا سا پریشر دے کر توڑیں۔
- اس طریقے سے ایمپیول (بینگ) با حفاظت اور آسانی سے ٹوٹ جائے گا۔

PRESENTATION
Opt-D Injection 5mg/ml: Pack of 1 Ampoule of 1ml.

INSTRUCTIONS
Use as advised by the physician
To be sold on the prescription of a registered medical practitioner only.
Keep all medicines out of the reach of children
Before using the product check on the absence of sediments.

STORAGE CONDITIONS:
Store below 25°C.
Protect from light, heat, moisture & freezing.

For suspected adverse drug reaction, report at reports@pharmevo.biz

For more information on our products
call PharmAssist helpline 0800-82222
Monday to Friday 9:00 am to 6:00 pm
or email us at : pharmassist@pharmevo.biz

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ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔
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صرف رجسٹرڈ ڈاکٹر کے نسخے پر ہی فروخت کی جائے۔
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