Miura-D™

[CHOLECALCIFEROL]

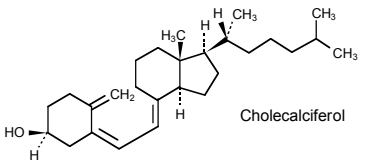
مائیورا۔ڈی

Vitamin D_3 Injection 5mg/mL (equivalent to 200,000 IU)

For oral and IM administration

DESCRIPTION

Miura-D (Cholecalciferol) is a fat soluble vitamin and is a precursor of the active hormone 1, 25-dihydroxy Cholecalciferol, also known as Calcitriol. Chemically it is 9, 10-Secocholesta-5, 7, 10 (19)-trien-3-ol,(3ß, 5Z,7E)-Cholecalciferol. Its molecular formula is $C_{27}H_{44}O$ and the structural formula is;



Cholecalciferol

QUALITATIVE & QUANTITATIVE COMPOSITION

Miura-D (Cholecalciferol) Injection is available for oral and IM administration as:

Miura-D Injection 5mg/mL
Each mL contains:
Cholecalciferol BP... 5mg
(Equivalent to 200,000 IU)

CLINICAL PHARMACOLOGY

Mechanism of Action

Calcitriol, which is the metabolite of cholecalciferol, exerts its effect by binding to the vitamin D receptors (VDRs) which are widely distributed through many body tissues. Cholecalciferol also has anti-osteoporotic, immunomodulatory, anticarcinogenic, antipsoriatic, antioxidant & mood-modulatory activities and along with parathyroid hormone & calcitonin it regulates serum calcium concentration.

Pharmacokinetics

Absorption

Cholecalciferol is well absorbed from the small intestine. Presence of bile is essential for adequate intestinal absorption. Absorption is reduced in liver or biliary disease.

Distribution

Cholecalciferol is bound to a specific α-globulin and albumin in plasma. It can be stored in adipose & muscle tissue for long periods of time and it may distribute into breast milk.

Metabolism

Cholecalciferol is hydroxylated in the liver by the enzyme vitamin D 25-hydroxylase to form 25-hydroxycholecalciferol (calcifediol). Calcifediol is then hydroxylated in the kidneys by the enzyme vitamin D_1-hydroxylase to form the active metabolites 1,25-dihydroxycholecalciferol (calcitriol). Calcitriol is further metabolised in the kidneys, including the formation of the 1,24,25-trihydroxy derivatives.

Excretion

Cholecalciferol is excreted mainly in the bile & feces with only small amounts appearing in urine. Elimination half life of calcitriol is 5 to 8 hours. Pharmacological activity persists for 3 to 5 days.

Special Population

Renal Impairment:

The elimination half life of calcitriol will increase by atleast two folds in chronic renal failure and hemodialysis patients compared with healthy subjects. Peak serum levels in patients with nephritic syndrome were reached in 4 hours. For patients requiring hemodialysis, peak serum levels were reached in 8 to 12 hours; half lives were estimated to be 16.2 and 21.9 hours, respectively.

THERAPEUTIC INDICATIONS

Miura-D (Cholecalciferol) is indicated in the prevention and treatment of vitamin D deficiencies.

DOSAGE AND ADMINISTRATION

Miura-D (Cholecalciferol) Injection 5mg/mL can be administered orally or by IM route 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 or children 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 once at the end of a month if the final trimester starts up in winter or in case of non 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:**
  0.5mL 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.

ADVERSE REACTIONS

Hyperphosphatemia or hypercalcemia (in excessive intake) and associated effects of hypercalcemia include hypercalciuria, ectopic calcification, renal & CV damage.

CONTRAINDICATIONS

Cholecalciferol is contraindicated in:

- Hypersensitivity to any of the components of the product.
- Hypercalcemia, hypercalciuria, calcium lithiasis.
- Kidney insufficiency or renal impairment.

PRECAUTIONS

- Treatment with cholecalciferol must be discontinued, if hypercalcemia and hypercalciuria occur.
- Caution must be taken if patient:
  - Had an allergic reaction to vitamin D
  - Has high levels of blood calcium or vitamin D
- Total doses of Cholecalciferol must be taken into consideration in case of simultaneous intake of other drugs containing this vitamin, to avoid any over dosage.
- In malabsorption.
- Avoid using vitamins or mineral supplements and antacids unless prescribed by a physician.

Pregnancy and Nursing mothers

Cholecalciferol can be prescribed during pregnancy & to nursing mothers if necessary, when used in daily amounts below 2000 IU.

Drug Interactions

- There is increased risk of hypercalcemia, if cholecalciferol is given with thiazide diuretics, calcium or phosphate.
- Cholecalciferol requirements may increase while using antiepileptics (e.g. carbamazepine, phenobarbitone, phenytoin & primidone).
- Rifampicin & isoniazid may reduce the efficacy of Cholecalciferol.
- Cholecalciferol effect may be counteracted by the use of corticosteroids, digoxin or any cardiac glycoside. Absorption of cholecalciferol may be reduced when taken with cholestyramine, colestipol, mineral oil, orlistat and ketoconazole.

OVERDOSAGE

Symptoms

In the event of an overdose, the symptoms that may occur include headache, fatigue, weight loss, growth retardation, anorexia, drowsiness, dry skin, itchy skin, nausea, vomiting, constipation, muscle or bone pain, metallic taste in the mouth, hypercalcemia, hypercalciuria, hyperphosphatemia, hyperphosphaturia, intense thirst, polyuria, arterial hypertension, dehydration and severe pain in upper stomach spreading to back or fainting.

Treatment

Overdosage can be treated by discontinuing administration of cholecalciferol, increasing diuresis or by increasing the administration of fluids.

STORAGE

Store below 25°C.
Protect from light and excessive heat.
Do not freeze.

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

HOW SUPPLIED

Miura-D (Cholecalciferol) 5mg/mL Injection is available in pack of 1x1mL ampoule.

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.

Manufactured by:

Getz pharma (PVT) LIMITED
www.getzpharma.com

29-30/27,
K.I.A., Karachi,
Pakistan

L00-200007562