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

D-360

1. **Generic Name**

Cholecalciferol Capsules U.S.P. 60,000 IU

2. **Qualitative and quantitative Composition:**

Each soft gelatin capsule contains:

Cholecalciferol (Vitamin D3) I.P. ……60,000 I.U.

Appropriated overages of vitamin added to compensate for loss on storage.

Approved colours used in capsules shell.

The list of excipients used are Gelatin, Glycerin, Isopropyl alcohol, Light Liquid paraffin, Mix Xylene, Soyabean Oil.

3. **Dosage form and strength**

Dosage form: Soft gelatin capsule

Strength: 60,000 I.U.

4. **Clinical particulars**

4.1. Therapeutic indication

For the treatment of vitamin D deficiency in:

- Hypophosphataemic rickets and osteomalacia
- Postgastrectomy and intestinal malabsorption osteomalacia
- Osteomalacia associated with prolonged use of anticonvulsants and other hepatic microsomal enzyme-inducing drugs
- Osteomalacia associated with hepatobiliary disorders

As an adjuvant in the management of chronic disease state in which vitamin D deficiency is Suspected such as CVD, Diabetes, Cancer (breast, prostate and colon), infectious diseases, TB and COPD.

4.2. Posology and method of administration

Posology

For the treatment of simple nutritional deficiencies cholecalciferol is generally preferred. A dose of 400 units daily is generally sufficient in adults for the prevention of simple deficiency states; 800 units daily is recommended in those whose exposure to sunlight is limited, in those whose diet is deficient in vitamin D, and in housebound or institutionalized elderly people. Deficiency due to malabsorption states or liver disease often requires higher doses for treatment, of up to 40 000 units daily. Doses of up to 200 000 units daily may be used in the treatment of hypocalcaemia due to hypoparathyroidism.

Method of administration

They are usually given orally.

4.3. Contraindications

This formulation contraindicated in the patient known to be hypersensitive (allergic) to Vitamin D used in this formulation. In patients with hypercalcemia, malabsorption syndrome, abnormal sensitivity to the toxic effects of vitamin D, and hypervitaminosis D.

4.4. Special warnings and precautions for use

WARNING

Hypersensitivity to vitamin D may be one etiologic factor in infants with idiopathic hypercalcemia. In these cases vitamin D must be strictly restricted.

PRECAUTIONS

Vitamin D should not be given to patients with hypercalcaemia. It should be used with caution in infants, who may have increased sensitivity to its effects, and patients with renal impairment or calculi, or heart disease, who might be at increased risk of organ damage if hypercalcaemia occurred. Plasma phosphate concentrations should be controlled during vitamin D therapy to reduce the risk of ectopic calcification. It is advised that patients receiving pharmacological doses of vitamin D should have their plasma-calcium concentration monitored at regular intervals, especially initially or if symptoms suggest toxicity. Similar monitoring is recommended in infants if they are breast fed by mothers receiving pharmacological doses of vitamin D.

4.5. Drugs interactions

There is an increased risk of hypercalcaemia if vitamin D is given with thiazide diuretics, calcium, or phosphate. Plasma-calcium concentrations should be monitored in such situations. Some antiepileptics may increase vitamin D requirements (e.g. carbamazepine, phenobarbital, phenytoin, and primidone). Rifampicin and isoniazid may reduce the effectiveness of vitamin D. Corticosteroids may counteract the effect of vitamin D.

Ketoconazole may inhibit the metabolism of paricalcitol and these drugs should be used with caution together; care should be taken when using paricalcitol with other potent inhibitors of the cytochrome P450 isoenzyme CYP3A4. Mineral oil interferes with the absorption of fat-soluble vitamins, including vitamin D preparations.

4.6. Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy

Hypercalcaemia during pregnancy may produce congenital disorders in the offspring, and neonatal hypoparathyroidism. However, the risks to the fetus of untreated maternal hypoparathyroidism are considered greater than the risks of hypercalcaemia due to vitamin D therapy.

Breast feeding

Vitamin D is distributed into breast milk, and its concentration appears to correlate with the amount of vitamin D in the serum of exclusively breast-fed infants. The infant be closely

monitored for hypercalcaemia or clinical manifestations of vitamin D toxicity if the mother is taking pharmacological doses of vitamin D.

4.7. Effects on ability to drive and use machines

D360 has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

Excessive intake of vitamin D leads to the development of hyperphosphataemia or hypercalcaemia. Associated effects of hypercalcaemia include hypercalciuria, ectopic calcification, and renal and cardiovascular damage. Symptoms of overdosage include anorexia,

lassitude, nausea and vomiting, constipation or diarrhoea, polyuria, nocturia, sweating, headache, thirst, somnolence, and vertigo. Interindividual tolerance to vitamin D varies considerably; infants and children are generally more susceptible to its toxic effects. The vitamin should be withdrawn if toxicity occurs. It has been stated that vitamin D dietary supplementation may be detrimental in persons already receiving an adequate intake through diet and exposure to sunlight, since the difference between therapeutic and toxic concentrations is relatively small.

The most potent forms of vitamin D, such as alfacalcidol and calcitriol, might reasonably be expected to pose a greater risk of toxicity; however, their effects are reversed rapidly on withdrawal. Hypersensitivity reactions have occurred. Skin irritation or contact dermatitis has been reported with topical preparations.

Hypercalcaemia: Vitamin D is the most likely of all vitamins to cause overt toxicity. Doses of 60000 units daily can cause hypercalcaemia, with muscle weakness, apathy, headache, anorexia, nausea and vomiting, bone pain, ectopic calcification, proteinuria, hypertension, and cardiac arrhythmias. Chronic hypercalcaemia can lead to generalised vascular calcification, nephrocalcinosis, and rapid deterioration of renal function. Hypercalcaemia has been reported in a patient after brief industrial exposure to colecalciferol.

A study in children treated for renal osteodystrophy has provided some evidence that hypercalcaemia may occur more frequently with calcitriol than with ergocalciferol. Another such study has suggested that vitamin D has nephrotoxic properties independent of the degree of induced hypercalcaemia, and that the decline in renal function may be more marked with calcitriol. Topical calcitriol may affect calcium homoeostasis, and hypercalcaemia has been reported in some studies. Hypervitaminosis D is characterized by effects on the following organ system:

Renal: Impairment of renal function with polyuria, nocturia, polydipsia, hypercalciuria, reversible azotemia, hypertension, nephrocalcinosis, generalized vascular calcification, or irreversible renal insufficiency which may result in death.

CNS: Mental retardation.

Soft Tissues: Widespread calcification of the soft tissues, including the heart, blood vessels, renal tubules, and lungs.

Skeletal: Bone demineralization (osteoporosis) in adults occurs concomitantly. Decline in the average rate of linear growth and increased mineralization of bones in infants and children (dwarfism), vague aches, stiffness, and weakness.

Gastrointestinal: Nausea, anorexia, constipation.

Metabolic: Mild acidosis, anemia, weight loss.

Reporting of adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report suspected adverse reactions via any point of contact available at www.torrentpharma.com.

4.9. Overdose

Human experience of overdose with D360 is limited.

5. Pharmacological properties

5.1. Mechanism of Action

The effects of administered vitamin D can persist for two or more months after cessation of treatment.

Hypervitaminosis D is characterized by:

Hypercalcemia with anorexia, nausea, weakness, weight loss, vague aches and stiffness, constipation, mental retardation, anemia, and mild acidosis.

Impairment of renal function with polyuria, nocturia, polydipsia, hypercalciuria, reversible azotemia, hypertension, nephrocalcinosis, generalized vascular calcification, or irreversible renal insufficiency which may result in death. Widespread calcification of the soft tissues, including the heart, blood vessels, renal tubules, and lungs. Bone demineralization (osteoporosis) in adults occurs concomitantly. Decline in the average rate of linear growth and increased mineralization of bones in infants and children (dwarfism).

The treatment of hypervitaminosis D with hypercalcemia consists of immediate withdrawal of the vitamin, a low calcium diet, generous intake of fluids, along with symptomatic and supportive treatment. Hypercalcemic crisis with dehydration, stupor, coma, and azotemia requires more vigorous treatment. The first step should be hydration of the patient. Intravenous saline may quickly and significantly increase urinary calcium excretion. A loop diuretic (furosemide or ethacrynic acid) may be given with the saline infusion to further increase renal calcium excretion. Other reported therapeutic measures include dialysis or the administration of citrates, sulfates, phosphates, corticosteroids, EDTA (ethylenediaminetetraacetic acid), and mithramycin via appropriate regimens. With appropriate therapy, recovery is the usual outcome when no permanent damage has occurred. Deaths via renal or cardiovascular failure have been reported.

5.2. Pharmacodynamic properties

The *in vivo* synthesis of the major biologically active metabolites of vitamin D occurs in two steps. The first hydroxylation takes place in the liver (to 25-hydroxy vitamin D) and the second in the kidneys (to 1, 25-dihydroxy- vitamin D). Vitamin D metabolites promote the active absorption of calcium and phosphorus by the small intestine, thus elevating serum calcium and phosphate levels sufficiently to permit bone mineralization. Vitamin D metabolites also mobilize calcium and phosphate from bone and probably increase the reabsorption of calcium and perhaps also of phosphate by the renal tubules. There is a time lag of 10 to 24 hours

between the administration of vitamin D and the initiation of its action in the body due to the necessity of synthesis of the active metabolites in the liver and kidneys. Parathyroid hormone is responsible for the regulation of this metabolism in the kidneys.

5.3. Pharmacokinetic properties

Vitamin D substances are well absorbed from the gastrointestinal tract. The presence of bile is essential for adequate intestinal absorption; absorption may be decreased in patients with decreased fat absorption.

Vitamin D and its metabolites circulate in the blood bound to a specific α-globulin. Vitamin D can be stored in adipose and muscle tissue for long periods of time. It is slowly released from such storage sites and from the skin where it is formed in the presence of sunlight or ultraviolet light. Cholecalciferol have a slow onset and a long duration of action; calcitriol and its analogue alfacalcidol, however, have a more rapid action and shorter half-lives. Cholecalciferol is hydroxylated in the liver by the enzyme vitamin D 25 - hydroxylase to form 25-hydroxycholecalciferol (calcifediol). These compounds undergo further hydroxylation in the kidneys by the enzyme vitamin D 1-hydroxylase to form the active metabolites 1, 25-dihydroxycholecalciferol (calcitriol).

Further metabolism also occurs in the kidneys, including the formation of the 1,24,25-trihydroxy derivatives. 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. Certain vitamin D substances may be distributed into breast milk.

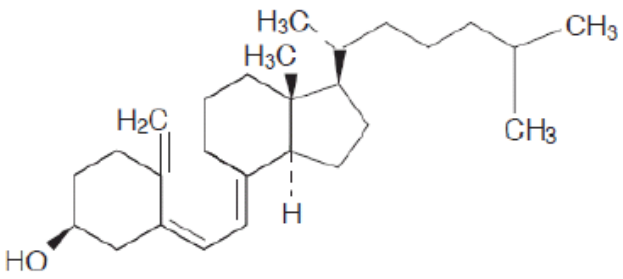
6. Nonclinical properties

6.1. Animal Toxicology or Pharmacology

There is no information found.

7. Description

Cholecalciferol is (5Z,7E)-(3S)-9,10-secocholesta -5,7,10(19)-triene-3-ol.The empirical formula is $C_{27}H_{44}O$ and its molecular weight is 384.6The structural formula of Cholecalciferol is:



D-360 Capsules

D-360 is Natural coloured oval shaped transparent soft gelatin capsules containing clear oily liquid.

The list of excipients used are Gelatin, Glycerin, Isopropyl alcohol, Light Liquid paraffin, Mix Xylene, Soyabean Oil.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than date of expiry.

8.3. Packaging information

D 360 Capsules are available in pack of 4 capsules.

8.4. Storage and handing instructions

Store in a dry place below $25^{O}C$.

Protect from light.

Keep out of reach of children.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

Softgel Healthcare PVT. LTD.

Survey No. 20/1, Kelambakkam Road,

Pudupakkam Village, 603103,

Vandalur Taluk, Chengalpattu District,

Tamilnadu.

11. Details of permission or licence number with date

Mfg. Lic. No. TN00002124, issue on 06.07.2024

12. Date of revision

MAR 2026

MARKETED BY

TORRENT PHARMA

TORRENT PHARMACEUTICALS LTD.

IN/D-360 Capsules/MAR 2026/02/PI