
D360 NANO SHOTS

1. Generic Name

Cholecalciferol (Vitamin D3) Oral Solution 60,000 IU

2. Qualitative and quantitative Composition:

D360 NANO SHOTS

Each 5 ml contains:

Cholecalciferol I.P.....60,000 IU

In a flavoured base..... q.s.

Colour: Tartrazine

The excipients used are Citric Acid Monohydrate, Sorbitol Glycerin, Mango Flavour Liquid, Mixed Fruit Liquid, Sodium Benzoate, Pineapple flavour liquid, Sucralose, Tartrazine Supra, Acrysol Ethylene Diamine Tetraacetic Acid.

3. Dosage form and strength

Dosage form: Oral solution

Strength: Cholecalciferol (Vitamin D3) 60,000 IU.

4. Clinical particulars

4.1. Therapeutic indication

It is indicated for the treatment of Vitamin D3 deficiency.

4.2. Posology and method of administration

Posology

Adults: Vitamin D3 60000 IU to be given once a week for a period of 8 weeks, followed by maintenance daily dose as directed by the physician.

Method of administration

Oral

It can be dispensed onto a spoon and taken as is or to facilitate the intake it can also be mixed with a small amount of cold or lukewarm food immediately prior to use. The patient should be sure to take the entire dose.

4.3. Contraindications

Contraindicated in patients with a hypersensitivity to any component of this product. Except under special circumstances, this medication should not be used when the following medical problems exist:

- Hypercalcaemia.
- Malabsorption syndrome.
- Hypervitaminosis D.
- Renal osteodystrophy with hyperphosphatemia (risk of metastatic calcification; however, vitamin D therapy can begin once serum phosphate levels have stabilized)

4.4. Special warnings and precautions for use

The risk–benefit should be considered when the following medical problems exist:

- Cholecalciferol should be used with caution in patients with renal impairment and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account. In patients with severe renal impairment, vitamin D in the form of cholecalciferol is not metabolized normally and another form of vitamin D should be used.
- During long-term treatment, serum and urinary calcium levels should be followed and renal function should be monitored through measurement of serum creatinine. Monitoring is especially important in elderly patients on concomitant treatment with cardiac glycosides or diuretics and in patients with a high tendency to calculus formation. Treatment must be reduced or suspended if urinary calcium exceeds 7.5 mmol/24 hours (300 mg/24 hours). In case of hypercalcaemia or signs of impaired renal function, treatment with cholecalciferol should be discontinued. Chronic or acute administration of excessive doses may lead to hypervitaminosis D, manifested by hypercalcemia and its sequelae.
- Vitamin D should be used with caution in patients with impairment of renal function and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account. In patients with severe renal insufficiency, cholecalciferol is not metabolised normally, and other forms of vitamin D should be used.
- The dose of cholecalciferol should be considered when prescribing other drugs containing vitamin D. Additional doses of calcium or vitamin D should be taken under close medical supervision. In such cases, it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.
- Cholecalciferol should be used with caution in patients suffering from sarcoidosis because of the risk of increased metabolism of vitamin D to its active metabolite. In these patients, serum calcium levels and urinary calcium excretion must be monitored.
- Cholecalciferol should be used with caution in immobilized patients with osteoporosis due to the increased risk of hypercalcaemia. The cholecalciferol treatment should be discontinued in prolonged immobilization and should only be resumed once the patient becomes mobile again.
- Conditions like arteriosclerosis or cardiac function impairment may be exacerbated due to the possibility of hypercalcaemia and elevated serum cholesterol concentrations.
- Cholecalciferol should be administered with caution in patients with hyperlipidaemia as it could potentially exacerbate Low-density lipoprotein LDL elevation. Administration of cholecalciferol in patients with hyperphosphatemia may put the patient at risk of metastatic calcification; normalization of phosphate levels indicated prior to therapy. Liver disease may, in turn, impair the absorption of cholecalciferol.

4.5. Drugs interactions

Cholestyramine

Cholestyramine has been reported to reduce intestinal absorption of fat-soluble vitamins; as such, it may impair intestinal absorption of vitamin D.

Phenytoin/Phenobarbital/Barbiturates

The co-administration of phenytoin or phenobarbital or barbiturates will not affect plasma concentrations of vitamin D but may reduce endogenous plasma levels of calcitriol by

accelerating metabolism. Since blood level of calcitriol will be reduced, higher doses of cholecalciferol may be necessary if these drugs are administered simultaneously.

Thiazides

Thiazides are known to induce hypercalcaemia by the reduction of calcium excretion in urine. Some reports have shown that the concomitant administration of thiazides with vitamin D causes hypercalcaemia. Therefore, precaution should be taken when co-administration is necessary.

Digitalis

Vitamin D dosage must be determined with care in patients undergoing treatment with digitalis, as hypercalcaemia in such patients may precipitate cardiac arrhythmias.

Ketoconazole

Ketoconazole may inhibit both synthetic and catabolic enzymes of vitamin D. Reductions in serum endogenous vitamin D concentrations have been observed following the administration of 300 mg/day to 1,200 mg/day ketoconazole for a week to healthy men. However, in vivo drug interaction studies of ketoconazole with vitamin D have not been investigated.

Corticosteroids

A relationship of functional antagonism exists between vitamin D analogues, which promote calcium absorption, and corticosteroids, which inhibit calcium absorption.

Phosphate-Binding Agents

Since vitamin D also has an effect on phosphate transport in the intestine, kidneys and bones, the dosage of phosphate-binding agents must be adjusted in accordance with the serum phosphate concentration.

Calcium Supplements

Uncontrolled intake of additional calcium-containing preparations should be avoided.

Ion exchange resins

Simultaneous treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D.

Magnesium

Magnesium-containing preparations (e.g. antacids) may cause hypermagnesemia and should, therefore, not be taken during therapy with vitamin D by patients on long-term renal dialysis.

Renal Impairment

In patients with severe renal impairment, vitamin D in the form of cholecalciferol is not metabolized normally and another form of vitamin D should be used.

Hepatic Impairment

Liver disease may impair the absorption of cholecalciferol.

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

Pregnancy Category A

Controlled studies in women have failed to demonstrate a risk to the foetus in the first trimester (and there is no evidence of a risk in later trimesters), and the possibility of foetal harm remains remote.

Maternal hypercalcaemia during pregnancy in humans may be associated with increased sensitivity to the effects of vitamin D, suppression of parathyroid function, or a syndrome of peculiar (elfin) facies, mental retardation and congenital aortic stenosis in infants.

Pregnancy Category D

If the dose is more than the recommended US RDA

There is positive evidence of human foetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g. if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).

Overdosage of vitamin D has been associated with foetal abnormalities in animals.

Lactation

Only small amounts of vitamin D metabolites appear in human milk. Infants who are totally breastfed and have little exposure to the sun may require vitamin D supplementation.

It is advised that patients receiving pharmacological doses of vitamin D should have their plasma-calcium concentration monitored at regular intervals, especially initially, and if the symptoms suggest toxicity, similar monitoring is recommended in infants if they are breastfed by mothers receiving vitamin D.

Geriatric Use

Studies have shown that the elderly may have an increased need for vitamin D due to a possible decrease in the capacity of the skin to produce previtamin D₃, or a decrease in exposure to the sun, or impaired renal function, or impaired vitamin D absorption.

4.7. Effects on ability to drive and use machines.

Vitamin D₃ has no influence on the ability to drive and use machines.

4.8. Undesirable effects

A very serious allergic/hypersensitivity reaction to this drug is rare. However, medical help may be needed in case of a serious allergic reaction, including rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, and trouble breathing. This is not a complete list of possible side effects.

Vitamin D at normal doses usually has no side effects. Too much vitamin D can cause harmful high calcium levels. Some of the associated symptoms are as follows: nausea/vomiting, constipation, loss of appetite, increased thirst, increased urination, mental/mood changes, and unusual tiredness.

Toxicity is much more likely to occur from high intakes of dietary supplements containing vitamin D. Vitamin D toxicity can cause non-specific symptoms such as anorexia, weight loss, polyuria, and heart arrhythmias. More seriously, it can also raise blood levels of calcium, which leads to vascular and tissue calcification, with subsequent damage to the heart, blood vessels and the kidneys. The use of supplements of both calcium (1,000 mg/day) and vitamin D (400 IU) by postmenopausal women was associated with a 17% increase in the risk of kidney stones over 7 years in the Women's Health Initiative. A serum calcidiol concentration consistently >500 nmol/L (>200 ng/mL) is considered to be potentially toxic.

Vitamin D toxicity, including nephrocalcinosis/renal failure, hypertension, and psychosis, can occur with prolonged use of cholecalciferol; relatively low doses can produce toxicity in hypersensitive infants and children. Hypervitaminosis D is reversible upon discontinuation of treatment unless renal damage is severe. Chronic excessive dosing can also lead to impairment of renal function with polyuria, nocturia, polydipsia, hypercalciuria, reversible azotaemia,

hypertension, nephrocalcinosis, generalized vascular calcification, or irreversible renal insufficiency which may result in death. Other problems associated with long-term overdosage include worsening of GI symptoms, pancreatitis, psychotic symptomatology, mental retardation, widespread calcification of the soft tissues, including the heart, blood vessels, renal tubules, and lungs and bone demineralization (osteoporosis) in adults occurs concomitantly. It could cause decline in the average rate of linear growth, increased mineralization of bones in infants and children (dwarfism), vague aches, stiffness, and weakness, nausea, anorexia, constipation, mild acidosis, anaemia, and weight loss.

Most reports suggest a toxicity threshold for vitamin D of 10,000–40,000 IU/day and serum calcidiol levels of 500–600 nmol/L (200–240 ng/mL). While symptoms of toxicity are unlikely at daily intakes below 10,000 IU/day, the FNB pointed to emerging science from national survey data, observational studies and clinical trials suggesting that even lower vitamin D intakes and serum calcidiol levels might have adverse health effects over time. The FNB concluded that serum calcidiol levels above approximately 125–150 nmol/L (50–60 ng/mL) should be avoided, as even lower serum levels (approximately 75–120 nmol/L or 30–48 ng/mL) are associated with increases in all-cause mortality, greater risk of cancer at some sites like the pancreas, greater risk of cardiovascular events, and more falls and fractures among the elderly.

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

Overdosage can lead to hypervitaminosis, hypercalciuria and hypercalcaemia. Symptoms of hypercalcaemia may include anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, mental disturbances, polydipsia, polyuria, bone pain, nephrocalcinosis, renal calculi and, in severe cases, cardiac arrhythmias. Extreme hypercalcaemia may result in coma and death. Persistently high calcium levels may lead to irreversible renal damage and soft tissue calcification.

Treatment of Hypercalcaemia: The treatment with calcium must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A, vitamin D and cardiac glycosides must also be discontinued. Emptying of the stomach should be done in patients with impaired consciousness. Rehydration and, according to severity, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin, and corticosteroids must be initiated. Serum electrolytes, renal function and diuresis must be monitored. In severe cases, electrocardiogram (ECG) and central venous pressure should be followed.

5. Pharmacological properties

5.1. Mechanism of action

Cholecalciferol, also called as vitamin D₃, is produced naturally by ultraviolet irradiation of the provitamin, 7-dehydrocholesterol (a precursor of vitamin D) in the skin. Absorbed cholecalciferol requires metabolic activation. The circulating vitamin undergoes hydroxylation in the liver with the help of the enzyme, vitamin D 25-hydroxylase to form 25-hydroxycholecalciferol (calcidiol), which is the predominant circulating metabolite. Further hydroxylation in the kidneys (in response to need for phosphorus and calcium) forms 1,25-dihydroxycholecalciferol (calcitriol) with the help of 1 α -hydroxylase. Calcidiol possesses some intrinsic activity, but calcitriol is the most active vitamin D metabolite with respect to

initiating intestinal transport of calcium and phosphate and mobilizing calcium from bone. Calcitriol may prevent phosphaturia by inhibiting parathyroid hormone secretion. Conversion to calcitriol is stimulated by the parathyroid hormone, as well as decreases in serum inorganic phosphate levels. Reduced renal conversion of calcidiol to calcitriol contributes to altered calcium haemostasis and osteodystrophy in uraemia.

5.2. Pharmacodynamic properties

Vitamin D3 (cholecalciferol) is a fat-soluble vitamin that plays a crucial role in maintaining calcium and phosphate balance in the body, which is essential for healthy bone formation and various metabolic functions. Its pharmacodynamic effects are primarily mediated through its active form, **calcitriol** (1,25-dihydroxyvitamin D3). Cholecalciferol itself is biologically inactive and undergoes two hydroxylation steps to become active: first in the liver, where it is converted to 25-hydroxyvitamin D3 (calcidiol), and then in the kidneys, where it is converted to calcitriol.

Calcitriol exerts its effects by binding to the vitamin D receptor (VDR), a nuclear receptor found in various tissues. The calcitriol-VDR complex functions as a transcription factor, regulating the expression of genes involved in calcium and phosphate absorption and bone metabolism. In the intestines, calcitriol increases the absorption of calcium and phosphate by enhancing the expression of transport proteins. In the kidneys, it promotes calcium reabsorption in the distal tubules, helping to maintain serum calcium levels. In bone tissue, calcitriol plays a dual role: at physiological levels, it promotes bone mineralization, but at higher levels, it can stimulate bone resorption indirectly by increasing osteoclast activity through osteoblast signaling.

Additionally, calcitriol suppresses parathyroid hormone (PTH) secretion, which helps prevent excessive bone resorption. Beyond its role in mineral metabolism, vitamin D3 also has effects on the immune system, enhancing innate immunity and modulating adaptive immune responses. The onset of action is delayed due to the time required for metabolic activation, and the effects are long-lasting because vitamin D3 is stored in fat tissue and released slowly over time. However, excessive intake can lead to vitamin D toxicity, resulting in hypercalcemia, nausea, weakness, and potential soft tissue calcification due to elevated calcium and phosphate levels.

5.3. Pharmacokinetic properties

Absorption

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.

Distribution

Vitamin D and its metabolites circulate in the blood, bound to a specific alpha-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 has a slow onset and a long duration of action.

Metabolism

Cholecalciferol is converted in the liver by hydroxylation to the active form 25-hydroxycholecalciferol. It is then further converted in the kidneys to 1,25-dihydroxycholecalciferol. 1,25-dihydroxycholecalciferol is the metabolite responsible for increasing calcium absorption. Vitamin D that is not metabolized is stored in adipose and muscle tissues.

Excretion

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

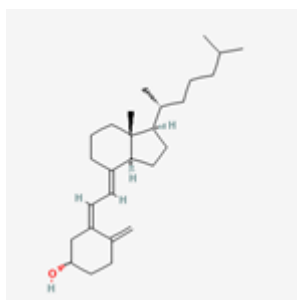
6.1. Animal Toxicology or Pharmacology

NA

7. Description

Cholecalciferol:

Cholecalciferol is (1S,3Z)-3-[(2E)-2-[(1R,3aS,7aR)-7a-methyl-1-[(2R)-6-methylheptan-2-yl]-2,3,3a,5,6,7-hexahydro-1H-inden-4-ylidene] ethylidene]-4-methylidenecyclohexan-1-ol. Its empirical formula is C₂₇H₄₄O and molecular weight is 384.6 g/mol the Chemical structure of:



D360 NANO SHOTS

D360 Nano Shots are Yellow coloured clear solution filled in amber glass bottle with flavoured odour. The excipients used are Citric Acid Monohydrate, Sorbitol Glycerin, Mango flavour liquid, Mixed Fruit Liquid, Sodium Benzoate, Pineapple Flavour Liquid, Sucralose, Tartrazine Supra, Acrysol Ethylene Diamine Tetraacetic Acid.

8. Pharmaceutical particulars

8.1. Incompatibilities

Not applicable

8.2. Shelf-life

Do not use later than date of expiry.

8.3. Packaging information

D360 NANO SHOTS is available in pack of 4 Bottles.

8.4. Storage and handing instructions.

Store at a temperature not exceeding 30°C. Protected from direct sunlight.

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

Ravenbhel Healthcare Pvt. Ltd.

At: EPIP, SIDCO, Kartholi,

Bari Brahmana, Jammu – 181133

11. Details of permission or licence number with date

Mfg. Licence. No: JK/01/17-18/LL/252 Issued on:27.02.2024

12. Date of revision

NA

MARKETED BY



TORRENT PHARMACEUTICALS LTD.

IN/ D360 NANO SHOTS 60,000 IU/DEC-2025/01/PI