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

SHELCAL 250

1. Generic Name:

Calcium and Vitamin D_3 Tablets

2. Qualitative and quantitative composition:

SHELCAL 250

Each film-coated tablet contains:

625 mg Calcium Carbonate from an Organic Source (Powdered Oyster Shell) equivalent to

Elemental Calcium 250 mg

Vitamin D3 I.P. 125 IU

Color: Titanium Dioxide I.P.

Appropriate overages of vitamins added to compensate for loss on storage

The Excipients Used are Powdered Oyster Shell, Microcrystalline Cellulose, Starch, Gelatin, Sodium Methyl Paraben, Propyl Paraben Sodium, Isopropyl Alcohol, Purified Water, Talc, Magnesium Stearate, Vitamin-D3 Granules, Ethyl Cellulose, Glycerol Mono-Oleate, Sucrose, Povidone, Sodium Carboxy Methylcellulose, Polysorbate 80,Colloidal Silicon Dioxide, Titanium Dioxide, Carnuba Wax

3. Dosage form and strength:

Dosage form: Tablet

Strength: 250 mg

4. Clinical particulars:

4.1 Therapeutic indication:

SHELCAL is indicated 'for the prevention and treatment of Calcium and Vitamin D3 deficiency'

4.2 Posology and method of administration:

Dosage instructions

Calcium and Vitamin D_3 film-coated tablet should be taken as directed by Physician.

4.3 Contraindications:

- Hypersensitivity to the active substances or to any of the excipients.
- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria (e.g. myeloma, bone metastases, primary hyperparathyroidism).
- Nephrolithiasis / nephrocalcinosis
- Severe renal impairment and renal failure
- Hypervitaminosis D
- Hypersensitivity to the active substances or to any of the excipients (including soya or peanut).

4.4 Special warnings and precautions for use:

During long-term treatment, serum calcium levels should be followed and renal function should

be monitored through measurements 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. In case of hypercalcaemia or signs of impaired renal function the dose should be reduced or the treatment discontinued. It is advisable to reduce or interrupt treatment temporarily if urinary calcium exceeds 7.5 mmol/24 h (300 mg/24 h).

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, vitamin D in the form of colecalciferol is not metabolised normally and other forms of vitamin D should be used.

Shelcal film-coated tablets should be prescribed with caution to patients suffering from sarcoidosis, due to the risk of increased metabolism of vitamin D into its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Shelcal film-coated tablets should be used with caution in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

The content of vitamin D (400 IU) in Shelcal film-coated tablets should be considered when prescribing other medicinal products 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. Milk-alkali syndrome (Burnett's syndrome), i.e. hypercalcaemia, alkalosis and renal impairment can develop when large amounts of calcium are ingested with absorbable alkali.

Shelcal film-coated tablets contain sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Drug-Interaction:

Thiazide diuretics reduce the urinary excretion of calcium. Due to increased risk of hypercalcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics.

Systemic corticosteroids reduce calcium absorption. During concomitant use, it may be necessary to increase the dose of Shelcal film-coated tablets.

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

Calcium carbonate may interfere with the absorption of concomitantly administered tetracycline preparations. For this reason, tetracycline preparations should be administered at least two hours before or four to six hours after oral intake of calcium.

Hypercalcaemia may increase the toxicity of cardiac glycosides during treatment with calcium and vitamin D. Patients should be monitored with regard to electrocardiogram (ECG) and serum calcium levels.

If a bisphosphonate or sodium fluoride is used concomitantly with Shelcal film-coated tablets, these medicinal products should be administered at least three hours before the intake of Shelcal film-coated tablet since gastrointestinal absorption may be reduced.

Rifampicin, phenytoin or barbiturates may reduce the activity of vitamin D3, since they increase the rate of its metabolism.

The absorption of quinolone antibiotics may be impaired if administered concomitantly with calcium. Quinolone antibiotics should be taken two hours before or six hours after intake of calcium.

Calcium salts may decrease the absorption of iron, zinc or strontium. Consequently, the iron, zinc or strontium preparation should be taken at a distance of two hours from the calcium preparation.

Calcium salts may reduce the absorption of the estramustin or thyroid hormones. It is recommended that taking Shelcal film-coated tablets be spaced at least 2 hours from these medicines.

Oxalic acid (found in spinach, sorrel and rhubarb) and phytic acid (found in whole cereals) may inhibit calcium absorption through formation of insoluble compounds with calcium ions. The patient should not take calcium products within two hours of eating foods high in oxalic acid and phytic acid.

4.6 Use in special populations

Pregnancy

Shelcal film-coated tablets may be given during pregnancy in cases of calcium and vitamin D3 deficiency.

During pregnancy the daily dose should not exceed 1500 mg of calcium and 600 IU of vitamin D. Animal studies have shown toxic effects on reproduction at high doses of vitamin D. In pregnant women, all calcium or vitamin D overdoses must be avoided as prolonged hypercalcaemia in pregnancy may lead to retardation of physical and mental development, supravalvular aortic stenosis and retinopathy in the child. There are no indications that Vitamin D3 at therapeutic doses is teratogenic in human.

Breast-feeding

Shelcal film-coated tablets can be used during breast-feeding. Calcium and vitamin D pass into breast milk. This should be considered when giving additional vitamin D to the child.

Fertility

There is no known harmful effect of endogenous levels of calcium and vitamin D in the normal range on fertility. There are no data available on the effect of Shelcal film-coated tablets on fertility.

Overdoses of vitamin D have shown teratogenic effects in pregnant animals. However, there have been no studies on the use of this medicinal product in human pregnancy and lactation. In humans, long term hypercalcaemia can lead to physical and mental retardation, aortic stenosis and retinopathy in a new born child. Vitamin D and its metabolites pass into the breast milk.

4.7 Effects on ability to drive and use machines:

There are no data the effect of this product on driving capacity and use of machines. An effect is, however, unlikely.

4.8 Undesirable effects:

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as:

Uncommon (>1/1,000 to <1/100); rare (>1/10,000 to <1/1,000) or very rare (<1/10,000).

Metabolism and nutrition disorders

Uncommon: Hypercalcaemia and hypercalciuria.

Very rare: Seen usually only in overdose, Milk-alkali syndrome

Gastrointestinal disorders

Rare: Constipation, flatulence, nausea, abdominal pain, and diarrhoea.

Very rare: Dyspepsia

Skin and subcutaneous disorders

Rare: Pruritus, rash and urticaria.

Other special population

Patients with renal impairment: potential risk of hyperphosphatemia, nephrolithiasis and nephrocalcinosis.

Reporting of side effects:

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:
http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

4.9 Overdose:

Overdose can lead to hypervitaminosis 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.

Milk-alkali syndrome may occur in patients who ingest large amounts of calcium and absorbable alkali. Symptoms are frequent urge to urinate, continuing headache, continuing loss of appetite, nausea or vomiting, unusual tiredness or weakness, hypercalcaemia, alkalosis and renal impairment.

Treatment of hypercalcaemia: The treatment with calcium and vitamin D must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A, vitamin D and cardiac glycosides must also be discontinued. Emptying of the stomach in patients with impaired consciousness. Rehydration, and, according to severity, isolated or combined treatment with loop diuretics,

bisphosphonates, calcitonin and corticosteroids. Serum electrolytes, renal function and diuresis must be monitored. In severe cases, ECG and CVP should be followed.

5. Pharmacological properties:

5.1 Pharmacodynamic properties:

Vitamin D increases the intestinal absorption of calcium.

Administration of calcium and vitamin D3 (colecalciferol) counteracts the increase of parathyreoid hormone (PTH), which is caused by calcium deficiency and which causes increased bone resorption.

A clinical study of institutionalised patients suffering from vitamin D deficiency indicated that a daily intake of two tablets of calcium 500 mg/Vitamin D 400 IU for six months normalised the value of the 25-hydroxylated metabolite of Vitamin D3 and reduced secondary hyperparathyroidism and alkaline phosphatases.

An 18-month double blind, placebo controlled study including 3270 institutionalised women aged 84±6 years that received supplementation of vitamin D (800 IU/day) and calcium phosphate (corresponding to 1200 mg/day of elemental calcium), showed a significant decrease of PTH secretion. After 18 month, an "intent-to treat" analysis showed 80 hip fractures in the calcium-vitamin D group and 110 hip fractures in the placebo group ($p=0.004$). A follow-up study after 36 months showed 137 women with at least one hip fracture in the calcium-vitamin D group ($n=1176$) and 178 in the placebo group ($n=1127$, $p<0.02$).

5.2 Pharmacokinetic properties:

Calcium

Absorption:

The amount of calcium absorbed through the gastrointestinal tract is approximately 30% of the swallowed dose.

Distribution and metabolism:

99% of the calcium in the body is concentrated in the hard structure of bones and teeth. The remaining 1% is present in the intra- and extracellular fluids. About 50% of the total blood-calcium content is in the physiologically active ionised form with approximately 10% being complexed to citrate, phosphate or other anions, the remaining 40% being bound to proteins, principally albumin.

Elimination:

Calcium is eliminated through faeces, urine and sweat. Renal excretion depends on glomerular filtration and calcium tubular reabsorption.

Vitamin D

Absorption:

Vitamin D3 is absorbed in the small intestine.

Distribution and metabolism:

Colecalciferol and its metabolites circulate in the blood bound to a specific globulin. Colecalciferol is converted in the liver by hydroxylation to the active form 25-hydroxycolecalciferol. It is then further converted in the kidneys to 1,25 hydroxycolecalciferol. 1,25 hydroxycolecalciferol is the metabolite responsible for increasing calcium absorption. Vitamin D which is not metabolised is stored in adipose and muscle tissues.

Elimination:

Vitamin D is excreted in faeces and urine.

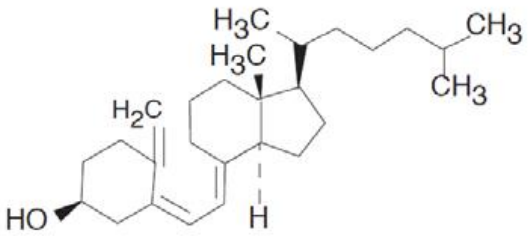
6. Nonclinical properties:

At doses far higher than the human therapeutic range teratogenicity has been observed in animal studies. There is further no information of relevance to the safety assessment in addition to what is stated in other parts of the SPC.

7. Description:

Vitamin D3 (Cholecalciferol)

White or almost white crystals, odourless or almost odourless.it is sensitive to air, heat and light. A reversible isomerisation to precholecalciferol may occur in solution, depending on temperature and time. Its empirical formula is $C_{27}H_{44}O$, and molecular weight is 384.6. It is chemically as (5Z, 7E)-(3S)-9, 10- secocholesta-5, 7, 10(19)-triene-3-ol.



Calcium (Precipitated Chalk)

Calcium A fine, white, microcrystalline powder. Its empirical formula is CaC03, and molecular weight is 100.1

8. Pharmaceutical particulars:

8.1 Incompatibilities:

Not applicable.

8.2 Shelf-life:

Do not use later than date of expiry.

8.3 Packaging information:

SHELCAL 250 is available in blister pack of 10x30 tablets.

8.4 Storage and handing instructions:

Store in a cool and dry place

9. Patient Counselling Information

Package leaflet: Information for the user

SHELCAL

Calcium Carbonate Vitamin D3 Tablets

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

What is in this leaflet?

9.1. What is and what it is used for

SHELCAL Contains Calcium Carbonate and Vitamin D_3.
Indication: 'for the prevention and treatment of Calcium and Vitamin D3 deficiency'

9.2. What you need to know before you use SHELCAL

Do not take SHELCAL:

- If you are hypersensitive to the active substances or to any of the excipients.
- If you have Kidney stone
- If you have kidney failure or severe Renal impairment
- If you have excessive amounts of Vitamin D in the blood
- If you have chronically increased calcium level in your urine or elevated blood-calcium level.
- Shelac contain hydrogenated soya oil. If you are allergic to peanut or soya, do not use this medicinal product.
- If you have osteoporosis due to prolonged immobilisation, renal stones.

Warnings and precautions:

Talk to your doctor or pharmacist before taking SHELCAL.
Tell your doctor or pharmacist:
If tou have kidney disease or impaired kidney function
If you have sarcoidosis (an inflammatory disease or unidentified origin characterised by formation of call agglomerates (lumps) in different locations).
If you are prone to development of kidney stone.
If you are an immobilised patient with osteoporosis.

Your doctor should decide whether calcium and /or vitamin D3 supply can be used in these conditions.
If you use shelcal film coated tablets in osteoporosis, your doctor may determine your blood-calcium level (calcaemia) before starting the treatment with the peoduct.
If you are on long- term treatment your doctor may, from time to time wish to check the level of calcium in your blood and take urine sample to monitor kidney function. Depending upon the results, your doctor may reduce the dosage or decide to discontinue the treatment.

Other medicines and SHELCAL

Tell your doctor or pharmacist if you are taking or recently taken any other medicines, including medicines obtained without a prescription.

9.3. How to use SHELCAL

Always take this medicine exactly as described in this leaflet or as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

If you take more SHELCAL than you should

You should only take what your doctor recommends. If you take too many SHELCAL tablets contact your doctor or pharmacist if you can do so. If not, go to the nearest hospital casualty department immediately, taking the SHELCAL pack and remaining tablets with you.

If you forget to take SHELCAL

If you forget to take your tablet, take it as soon as possible and continue to take the tablets as normal. Do not take a double dose to make up for a forgotten tablet.

If you stop taking SHELCAL

Always talk to your doctor or pharmacist before stopping using SHELCAL.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist

9.4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Frequency not known (frequency cannot be estimated from the available data):
Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as:

Uncommon (>1/1,000 to <1/100); rare (>1/10,000 to <1/1,000) or very rare (<1/10,000).

Metabolism and nutrition disorders

Uncommon: Hypercalcaemia and hypercalciuria.

Very rare: Seen usually only in overdose, Milk-alkali syndrome

Gastrointestinal disorders

Rare: Constipation, flatulence, nausea, abdominal pain, and diarrhoea.

Very rare: Dyspepsia

Skin and subcutaneous disorders

Rare: Pruritus, rash and urticaria.

<u>Other special population</u>

Patients with renal impairment: potential risk of hyperphosphatemia, nephrolithiasis and nephrocalcinosis.

Reporting of side effects:

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:
http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting

9.5. How to store SHELCAL

Store in a cool and dry place

9.6. Contents of the pack and other information

SHELCAL 250

The Excipients Used Are Powdered Oyster Shell, Microcrystalline Cellulose, Starch, Gelatin, Sodium Methyl Paraben, Propyl Paraben Sodium, Isopropyl Alcohol, Purified Water, Talc, Magnesium Stearate, Vitamin-D3 Granules, Ethyl Cellulose, Glycerol Mono-Oleate, Sucrose, Povidone, Sodium Carboxy Methylcellulose, Polysorbate 80,Colloidal Silicon Dioxide, Titanium Dioxide, Carnuba Wax

White Coloured, Round, Biconvex, Film Coated Tablets With Plain Surface on Both Side.

SHELCAL 250 is available in blister pack of 10x30 tablets.

10. Details of manufacturer

TORRENT PHARMACEUTICALS LTD. (UNIT-II)

Plot no: 725 & 726, 32 no. middle camp,

NH-10 East District, gangtok Sikkim -737135.

11. Details of permission or licence number with date

Mfg Lic No: M/786/2017 issued on 6 DEC 2021

12. Date of revision

MAY-2022

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/ SHELCAL 250 mg /MAY-22/02/PI