1.1 Product Name: VITOC-D SOFTGEL

(Cholecalciferol Capsules USP **)**

1.2 Pharmaceutical Dosage Form: Softgel Capsules

2. QUALITATIVE AND QUANTITATIVES COMPOSITION:

Each soft gelatin capsule contains:
Cholecalciferol USP…….1.5 mg ≅ 60000 IU
Excipients: q.s.

Qualitative and Quantitative Formula:

Sr. No.	Ingredients	Label Claim	Overages	Qty. Input mg/cap
1.1 Gelatin Mass Preparation:				
1.	Gelatin BP	-	-	262.5
2.	Glycerin BP	-	-	75.0
3.	Sorbitol Solution 70% (Non-Crystallizing) BP	-	-	50 .0
4.	Methyl Paraben BP	-	-	1.25
5.	Propyl Paraben BP	-	-	0.313
			Total Weight →	389.06
1.2 Medicament Preparation:				
1.	Cholecalciferol (Vitamin D_3) USP	60000 IU	10 %	1.65
2.	Butylated Hydroxy Anisole BP	-	-	0.25
3.	Butylated Hydroxytoluene BP	-	-	0.25
4.	Refined Soyabean Oil USP	-	-	217.85
			Total Weight →	220.0

3. Pharmaceutical Form Visual Description of the Appearance of the Product:

A natural, transparent oval shaped soft gelatin capsules containing slightly yellowish oily liquid.

4. Clinical Particulars

4.1 Therapeutic indications

The prevention and treatment of vitamin D deficiency.

As an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency.

Vitoc-D is indicated in adults, the elderly and adolescents.

Any of the following symptoms may represent vitamin D deficiency (associated with weak and fragile bones):

- Muscle pain and muscle cramp
- Chronic back pain
- Bone and joint pain
- Fatigue and weakness

4.2 Posology and method of administration

Posology:

Adults:

▪ Treatment of vitamin D deficiency: 60000 IU/week (1 capsule) for 7 weeks, followed by maintenance therapy (equivalent to 1000 IU/day, such as 1 capsule per month, may be required. Follow-up 25(OH)D measurements should be made approximately three to four months after initiating maintenance therapy to confirm that the target level has been achieved)

Method of administration:

Oral - The capsules should be swallowed whole with water.

Patients should be advised to take Cholecalciferol Capsules preferably with a meal (see section Pharmacokinetic properties - "Absorption").

4.3 Contraindications

▪ Hypersensitivity to cholecalciferol or other excipients of Cholecalciferol Capsules.

▪ Hypercalcaemia and/or hypercalciuria.

▪ Nephrolithiasis, or patients who are susceptible to form calcium-containing renal calculi (kidney stone).

▪ Severe renal impairment.

▪ Cholecalciferol Capsules must not be used in children (under 12 years) due to their inability to swallow capsules and/or the potential risk of choking.

▪ Hypervitaminosis D.

4.4 Special warnings and precautions for use

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 Cholecalciferol is not metabolised normally and other forms of vitamin D should be used.

Caution is required in patients receiving treatment for cardiovascular disease.

Vitoc-D 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.

Allowances should be made for vitamin D supplements from other sources.

The need for additional 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.

This medicine contains arachis oil (peanut oil). If you are allergic to peanut or soya, do not use this medicinal product.

Vitoc-D should not be given to children.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with phenytoin or barbiturates can decrease the effect of vitamin D because of metabolic activation. Concomitant use of glucocorticoids can decrease the effect of vitamin D.

The effects of digitalis and other cardiac glycosides may be accentuated with the oral administration of calcium combined with Vitamin D. Strict medical supervision is needed and, if necessary monitoring of ECG and calcium.

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

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.

4.6 Fertility, pregnancy and lactation

There are no or limited amount of data from the use of Cholecalciferol in pregnant women. Studies in animals have shown reproductive toxicity. The recommended daily intake for pregnant women is 400 IU, however, in women who are considered to be vitamin D deficient a higher dose may be required. 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 Vitamin D and its metabolites are excreted in breast milk. Overdose in infants induced by nursing mothers has not been

observed; however, when prescribing additional vitamin D to a breast-fed child the practitioner should consider the dose of any additional vitamin D given to the mother.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: uncommon (>1/1,000, <1/100) or rare (>1/10,000, <1/1,000).

Metabolism and nutrition disorders.

Uncommon: Hypercalcaemia and hypercalciuria.

Skin and subcutaneous disorders.

Rare: Pruritus, rash and urticaria.

4.9 Overdose

Discontinue Cholecalciferol Capsules when calcaemia exceeds 10.6 mg/dl (2.65 mmol/l) or if the calciuria exceeds 300 mg/24 hours in adults or 4-6 mg/kg/day in children. An overdose manifests as hypercalcaemia and hypercalciuria, the symptoms of which include the following: nausea, vomiting, thirst, constipation, polyuria, polydipsia and dehydration.

Chronic overdosage may lead to vascular and organ calcification, as a result of hypercalcaemia.

Treatment in cases of overdose

Discontinue administration of Cholecalciferol Capsules and initiate rehydration.

5. Pharmacological Properties

Pharmacotherapeutic group: Cholecalciferol (vitamin D and analogues)

ATC code: A11C C05

5.1 Pharmacodynamic properties

In its biologically active form Vitamin D 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 vitamin D_3. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active vitamin D.

5.2 Pharmacokinetic properties

The pharmacokinetics of vitamin D is well known.

Absorption

Vitamin D is well absorbed from the gastro-intestinal tract in the presence of bile, so the administration with the major meal of the day might therefore facilitate the absorption of Vitamin D.

Distribution and biotransformation

It is hydroxylated in the liver to form 25-hydroxy-cholecalciferol and then undergoes further hydroxylation in the kidney to form the active metabolite 1, 25-dihydroxy-cholecalciferol (calcitriol).

Elimination

The metabolites circulate in the blood bound to a specific α – globin, vitamin D and its metabolites are excreted mainly in the bile and faeces.

Characteristics in Specific Groups of Subjects or Patients

A 57% lower metabolic clearance rate is reported in subjects with renal impairment as compared with that of healthy volunteers.

Decreased absorption and increased elimination of vitamin D occurs in subjects with malabsorption.

Obese subjects are less able to maintain vitamin D levels with sun exposure and are likely to require larger oral doses of vitamin D to replace deficits.

5.3 Preclinical safety data

No remarkable findings.

6. Pharmaceutical Particulars

(a) List of Excipients

Sr. No.	Ingredients	Specification
1	Gelatin	BP
2	Glycerin	BP
3	Sorbitol Solution 70% (Non-Crystallizing)	BP
4	Methyl Paraben	BP
5	Propyl Paraben	BP
6	Butylated Hydroxyanisole	BP
7	Butylated Hydroxytoluene	BP
8	Refined Soyabean Oil	USP

(b) Incompatibilities: Not applicable

(c) Shelf Life: 24 Months

(d) Special Precautions for Storage:

Store at a temperature below 30°C. Protect from light.
Keep medicine out of reach of children.

(e) Nature and Contents of Container:

Alu-Alu Blister of 2 x 4's Capsules along with pack insert are packed in inner carton.
Such 10 inner cartons are packed in outer carton.

7. Name and Address of Manufacturer

Name of Manufacturer	**:**	**M/S INDCHEMIE HEALTH SPECIALITIES PVT. LTD.**
Address of manufacturer	**:**	**Indchemie Health Specialities Pvt. Ltd.** Unit-II, Amaliya, Daman 659/B, Somnath Kevdi Road, Dabhel, Daman-396 210. INDIA
Particulars of applicant	**:**	**CACHET PHARMACEUTICALS PRIVATE LIMITED**
Address of applicant	**:**	415, Shah Nahar Ind. Estate, Dr. E.Moses Road, Worli, Mumbai-400 018 Maharashtra, India

8. Marketing authorization holder

Cachet Pharmaceuticals Pvt. Ltd.

415, Shah Nahar Industrial Estate,

Dr. E. Moses Road, Worli, Mumbai - 400 018,

Maharashtra, India.

9. Marketing authorization number(s)

Not Applicable.

10. Date of first authorization/renewal of the authorization

Not Applicable.