1. PRODUCT NAME

Vit.D3, 1.25mg (equivalent to 50,000IU), soft gelatin capsules.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Vit.D3 soft gelatin capsule contains Colecalciferol (Vitamin D3) 1.25mg (equivalent to 50,000IU).

All ingredients of animal origin including the gelatin capsule are halal compliant.

Contains soya oil and sulfites.

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Vit.D3 capsules are presented as natural coloured, transparent, oval shaped, soft gelatin capsules, containing pale yellow coloured oil.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

The treatment of vitamin D deficiency in adults.
The prevention of vitamin D deficiency in high-risk adults.

4.2 Dose and method of administration

Treatment of **moderate/severe** vitamin D deficiency (less than 10 mcg/L of serum 25-hydroxyvitamin D concentration):
Dosage = 50,000 IU (1 x colecalciferol capsule) daily for 10 days, then 50,000 IU (1 x colecalciferol capsule) each month.

Treatment of **mild/moderate** vitamin D deficiency (10mcg/L or higher):
Dosage = 50,000 IU (1 x colecalciferol capsule) each month.

Prevention of vitamin D deficiency in high-risk adults:
Dosage = 50,000 IU (1 x colecalciferol capsule) every 2 to 3 months.

Paediatric population

See section 4.3.

4.3 Contraindications

- Colecalciferol is contraindicated in patients with hypersensitivity to any component of this product. Vit.D3 capsules contain soya oil. If you are allergic to peanut or soya, do not use this product.

- Hypercalcaemia
- Hypervitaminosis D
- Diseases or conditions which could lead to hypercalcaemia and / or hypercalciuria.
- Severe renal impairment
- Nephrolithiasis
- Pregnancy
- Lactation
- Children under 18 years of age

4.4 Special warnings and precautions for use

Vit.D3 should be used with caution in the following populations:

- Arteriosclerosis or cardiac function impairment (conditions may be exacerbated due to possibility of hypercalcaemia and elevated serum cholesterol concentrations).
- Sarcoidosis, and possibly other granulomatous diseases (increased sensitivity to effects of vitamin D). These patients should be monitored with regard to the calcium content in serum and urine.

Monitoring

25-hydroxyvitamin D concentration, calcium, phosphate, parathyroid hormone, and alkaline phosphatase (ALP) monitoring should be considered for populations at high risk of vitamin D deficiency such as:

- Institutionalised or hospitalised elderly individuals
- Dark-skinned individuals
- Individuals with limited effective sun exposure due to protective clothing or consistent use of sunscreens
- Individuals with malabsorption, including inflammatory bowel disease and coeliac disease
- Obese individuals
- Patients being evaluated for osteoporosis

Renal impairment

Caution is required in patients with impairment of renal function. Toxicity may occur in patients receiving Vitamin D3 for non-renal problems, although toxicity is also possible during treatment of renal osteodystrophy because of increased requirements and decreased renal function.

Vitamin D3 should not be used in patients with severe renal impairment (see section 4.3).

The effect on calcium and phosphate levels should be monitored.

Hepatic impairment
No dose adjustment is required in patients with hepatic impairment.

Safety information for long-term administration of doses
Allowances should be made for the total dose of Vitamin D3 in cases associated with treatments already containing Vitamin D3, foods enriched with Vitamin D3, cases using milk enriched with Vitamin D3, and the patient's level of sun exposure.

There is no clear evidence for causation between Vitamin D3 supplementation and renal stones, but the risk is plausible, especially in the context of concomitant calcium supplementation. The need for additional calcium supplementation should be considered for individual patients. Calcium supplements should be given under close medical supervision.

4.5 Interaction with other medicines and other forms of interaction
Thiazide diuretics
There is an increased risk of hypercalcaemia if Vitamin D3 is co-administered with thiazide diuretics and calcium. Plasma-calcium concentrations should be monitored in patients receiving the drugs concurrently.

Anticonvulsants (e.g. Carbamazepine, Phenobarbitone, Phenytoin and Primidone)
Concomitant treatment with certain anticonvulsants can decrease the effects of Vitamin D3 because of metabolic activation.

Antacids, Colestipol, Cholestyramine, Mineral oil, Orlistat
Gastrointestinal absorption of Vitamin D3 may be impaired.

Calcium, Phosphate
There is an increased risk of hypercalcaemia if Vitamin D3 is given with calcium and phosphate. Calcium concentrations should be monitored in those situations.

Digoxin
Vitamin D3 should be used with caution in patients on digoxin as hypercalcaemia (which may result with Vitamin D3 use) may precipitate cardiac arrhythmias. Monitoring serum calcium concentration and ECG is recommended.

Corticosteroids
Systemic corticosteroids reduce calcium absorption, and the effect of Vitamin D3 may be decreased.

Rifampicin
Concomitant treatment with rifampicin can decrease the effect of Vitamin D3 because of metabolic activation.

Isoniazid
Isoniazid may reduce the effectiveness of colecalciferol.

Antifungal medicines
Antifungal medicines such as ketoconazole may interfere with Vitamin D3 activity by inhibition of the conversion to active form.

Actinomycin (cytotoxic agent)
Actinomycin may affect the breakdown of colecalciferol.

Warfarin
A case of severely decreased prothrombin has been reported as due to a possible interaction of Vitamin D3 with warfarin and calcium carbonate.

Different vitamin D analogues
Concomitant use of Vitamin D3 with vitamin D analogues, is not recommended due to the additive effect and increased toxic potential.

4.6 Fertility, pregnancy and lactation
Fertility
Fertility clinical data is not available (see section 5.3).

Pregnancy
Vit.D3 50,000 IU capsules should not be given to pregnant women and a lower strength formulation should be used.

There are no or limited data available on the use of colecalciferol in pregnant women. Overdose of vitamin D has been associated with foetal abnormalities in animals. The recommended daily intake for pregnant women is generally 400 IU.

Lactation
Vit.D3 50,000 IU capsules are not suitable for breast feeding women.

Vitamin D and its metabolites are excreted in breast milk. Use in breast feeding does not replace the need for Vitamin D3 administration in the neonate.

4.7 Effects on ability to drive and use machines
Presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

4.8 Undesirable effects
Ingestion of excessive doses of vitamin D either as an acute dose or over prolonged periods can result in hyperphosphataemia or hypercalcaemia (see section 4.9).

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100), rare (≥ 1/10,000 to < 1/1,000), not known.

Gastrointestinal disorders
Not known: Dysphagia

General disorders and administration site conditions
Not known: Face oedema

Investigations
Not known: Prothrombin decreased (see section 4.5 Warfarin)

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia and hypercalciuria

Reproductive system and breast disorders
Not known: Oedema genital

Respiratory, thoracic and mediastinal disorders
Not known: Choking

Skin and subcutaneous tissue disorders
Rare: Pruritus, rash and urticaria

Not known: Dry skin, nail disorder

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 Overdose
Colecalciferol (Vitamin D3) have a relatively low therapeutic index. Ingestion of excessive vitamin D either as an acute overdose or over prolonged periods can result in severe toxicity.

Death may occur as a result of renal or cardiovascular failure caused by vitamin D toxicity.

Excessive intake of vitamin D leads to the development of hypercalcaemia and its associated effects including hypercalciuria, hyperphosphataemia, ectopic calcification, and renal and cardiovascular damage.

Symptoms of overdosage include anorexia, lassitude, nausea, vomiting, diarrhoea, constipation, polyuria, sweating, headache, thirst, vertigo, muscle pain, joint pain, weight loss and in the final stage, dehydration.

Paediatric population
Infants and children may react sensitively to far lower concentrations and are generally more susceptible to its toxic effects. Growth may be arrested in children, especially after prolonged administration of 1800 IU Vitamin D3 per day.

Treatment of overdose
Hypervitaminosis D is treated by withdrawal of the vitamins, low-calcium diet, and generous fluid intake.

If hypercalcaemia persists, a low-calcium diet and prednisone may be started. Severe hypercalcaemia may be treated with calcitonin, etidronate, pamidronate, or gallium nitrate.

Hypercalcaemic crisis requires vigorous hydration with intravenous saline to increase calcium excretion, with or without a loop diuretic.

Cardiac arrhythmias may be treated with small doses of potassium with continuous cardiac monitoring.

Therapy may be reinstituted at a lower dose when serum calcium concentrations return to normal. Serum or urinary calcium levels should be obtained twice weekly after dosage changes.

For risk assessment and advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues, ATC code: A11CC05

Colecalciferol is a vitamin D compound which possesses the property of preventing or treating rickets.

Vitamin D is essential for promoting absorption and utilisation of calcium and phosphate and for normal calcification of bone. Along with parathyroid hormone and calcitonin, it regulates serum calcium concentrations by increasing serum calcium and phosphate concentrations as needed. Vitamin D stimulates calcium and phosphate absorption from the small intestine and mobilises calcium from bone.

Colecalciferol is transferred to the liver where it is converted to calcifediol (25-hydroxycolecalciferol), which is then transferred to the kidneys and converted to calcitriol (1,25-dihyroxycolecalciferol, thought to be the most active form) and 24,25-dihydroxycolecalciferol (physiologic role not determined).

Calcitriol appears to act by binding to a specific receptor in the cytoplasm of the intestinal mucosa and subsequently being incorporated into the nucleus, probably leading to formation of the calcium- binding protein which results in increased absorption of calcium from the intestine. Also, calcitriol may regulate the transfer of calcium ion from bone and stimulate reabsorption of calcium in the distal renal tubule, thereby effecting calcium homeostasis in the extracellular fluid.

Onset of action – Hypercalcaemic: 12 to 24 hours; therapeutic effect may take 10 to 14 days.

Duration of action – Following oral administration: up to 6 months; repeated doses have a cumulative action.

5.2 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 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. Ergocalciferol and colecalciferol 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.

Colecalciferol and ergocalciferol are hydroxylated in the liver by the enzyme vitamin D 25-hydroxylase to form 25-hydroxycolecalciferol (calcifediol) and 25-hydroxyergocalciferol respectively. These compounds undergo further hydroxylation in the kidneys by the enzyme vitamin D 1-hydroxylase to form the active metabolites 1,25-dihydroxycolecalciferol (calcitriol) and 1,25-dihydroxyergocalciferol respectively. Further metabolism also occurs in the kidneys, including the formation of the 1,24,25- trihydroxy derivatives. Of the synthetic analogues, alfacalcidol is converted rapidly in the liver to calcitriol, and dihydrotachysterol is hydroxylated, also in the liver, to its active form 25- hydroxydihydrotachysterol.

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.

5.3 Preclinical safety data

Studies with calcitriol have found no evidence of mutagenicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule shell

- Gelatin BP
- Glycerin BP
- Purified water BP

Capsule fill

- Refined Soya Oil BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

HDPE bottle: 36 Months
Blister pack: 36 Months

6.4 Special precautions for storage

Store below 25°C. Protect from light.

6.5 Nature and contents of container

HDPE bottle with child resistant closure and silica desiccant. Pack-size of 12 soft gelatin capsules.

PVC/Aluminium blisters in a carton. Pack-sizes of 12, 40 and 100 soft gelatin capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7. MEDICINE SCHEDULE

Prescription medicine

8. SPONSOR

Multichem NZ Limited
Private Bag 93527
Takapuna
AUCKLAND 0740
Telephone: (09) 488 0330

9. DATE OF FIRST APPROVAL

17 February 2014

10. DATE OF REVISION OF THE TEXT

06 May 2025

SUMMARY TABLE OF CHANGES

SECTION	CHANGE
4.9	Added “For risk assessment” to the information on the management of overdose.
6.5	Updated to include new blister pack sizes.