SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

1. Name of the medicinal product

Terad Caplet

2. Qualitative and quantitative composition

Each caplet contains Cholecalciferol (Vitamin D_3) 50, 0000 IU

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Caplet.

A white to off white coated caplet with AFRAB inscribed on one side and a marked line on the other.

4. Clinical particulars

4.1 Therapeutic indications

.Terad is indicated for prevention and treatment of vitamin D_3 deficiency and hypocalcaemia disorders such as hypoparathyroidism.

.Treatment of osteomalacia and ricket

.Treatment of corticosteroid induced osteoporosis.

.Treatment and prevention of osteoporosi with conjunction of calcium supplement.

.Treatment and prevention of bones fractures.

4.2 Posology and method of administration

Adult: one caplet (50,000IU) once weekly

Method of Administration

Oral administration only

4.3 Contraindications

Terad caplet must not be used in patients with:

- Hypersensitivity to the active substance (Colecalciferol) or to any of the excipients listed in section 6.1
- Hypercalcaemia and/or hypercalciuria
- Nephrolithiasis (Renal calculi)
- Hypervitaminosis
- Severe renal impairment

4.4 Special warnings and precautions for use

Terad caplet 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.

Terad caplet should not be taken by patients with a tendency to form calcium-containing renal calculi.

Caution is required in patients receiving treatment for cardiovascular disease

(see section 4.5 – cardiac glycosides including digitalis).

Terad caplet 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, other vitamin D containing medicines or 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.

Paediatric population

Terad caplet should not be given to infants and children under the age of 12.

4.5 Interaction with other medicinal products and other forms of interaction

Phosphate infusions should not be administered to lower hypercalcaemia of hypervitaminosis D because of the dangers of metastatic calcification.

Patients treated with cardiac glycosides may be susceptible to high calcium levels and should have ECG parameters and calcium levels monitored. It is recommended to reduce the dose or interrupt treatment if the calcium content in the urine exceeds 7.5 mmol/24 hours (300 mg/24 hours).

Simultaneous administration of benzothiadiazine derivatives (thiazide diuretics) increases the risk of hypercalcaemia because they decrease the calcium excretion in the urine. The calcium levels in plasma and urine should therefore be monitored for patients undergoing long-term treatment.

If Colecalciferol is combined with metabolites or analogues of vitamin D careful monitoring of serum calcium levels is recommended.

Anti-convulsants e.g. phenytoin, phenobarbital, primidone may diminish the effect of Colecalciferol due to hepatic enzyme induction.

Rifampicin may reduce the effectiveness of Colecalciferol due to hepatic enzyme induction.

Isoniazid may reduce the effectiveness of Colecalciferol due to inhibition of the metabolic activation of Colecalciferol.

Drugs leading to fat malabsorption, e.g. orlistat, liquid paraffin, cholestyramine, may impair the absorption of Colecalciferol.

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.

Concomitant use of glucocorticoids can decrease the effect of vitamin D.

4.6 Pregnancy and Lactation

Pregnancy

Terad caplet should not be used during pregnancy unless the clinical condition of the woman requires treatment with colecalciferol, at a dose necessary to overcome the deficiency.
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.
Based on human experience and animal studies, vitamin D overdose causes physical and mental disability and congenital heart and eye conditions, due to hypercalcaemia, when administered during pregnancy.

Breast-feeding
Colecalciferol 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 effects on the ability to drive or use machines have been performed. Colecalciferol has no known side effects that are likely to affect the ability to drive and use or operate machines.

4.8 Undesirable effects

Allergic reaction, like rash; hives; itching; red, swollen, blistered, or peeling skin with or without fever; wheezing; tightness in the chest or throat; trouble breathing, swallowing, or talking; unusual hoarseness; or swelling of the mouth, face, lips, tongue, or throat.
Signs of high calcium levels like weakness, confusion, feeling tired, headache, upset

stomach and throwing up, constipation, or bone pain.

4.9 Overdose

Acute or chronic overdose of Colecalciferol can cause hypercalcaemia, an increase in the serum and urinary concentrations of calcium. The symptoms of hypercalcaemia are not very specific and consist of nausea, vomiting, diarrhoea often in the early stages and later constipation, anorexia, fatigue, headache, muscle and joint pain, muscle weakness, polydipsia, polyuria formation of renal calculi, nephrocalcinosis, kidney failure, calcification of soft tissues, changes in ECG measurements, arrhythmias and pancreatitis. In rare and isolated cases there are reports that hypercalcaemia is fatal.

Treatment of overdose

A normalisation of hypercalcaemia due to vitamin D intoxication lasts several weeks. The recommendation for the treatment of hypercalcaemia is the avoidance of any further administration of vitamin D, including supplements, dietary intakes and the avoidance of sunlight. A low calcium or calcium-free diet can also be considered.

Rehydration and the treatment with diuretics e.g. furosemide to ensure adequate diuresis should be considered. Additional treatment with calcitonin or corticosteroids can also be considered.

Phosphate infusions should not be administered to lower hypercalcaemia of hypervitaminosis D because of the dangers of metastatic calcification.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues

ATC code: A11CC05

Absorption: Colecalciferol is easily absorbed in the small intestine.

Colecalciferol is produced within the skin under the influence of UV radiation including sunlight. In its biologically active form, Colecalciferol 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 Colecalciferol. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active Colecalciferol.

Elimination: Colecalciferol and other forms of vitamin D are excreted in faeces and urine.

5.2 Pharmacokinetic properties

The pharmacokinetics of Colecalciferol has been widely studied and are well-known. Colecalciferol from nutritional sources is almost completely absorbed from within the gastro- intestinal tract in the presence of dietary lipids and bile acids. Colecalciferol is stored in fat cells and its biological half-life is approximately 50 days.

Colecalciferol is metabolised by microsomal hydroxylase to form 25-hydroxycolecalciferol ($25(OH)D_3$, calcidiol), the primary storage form of vitamin D_3. $25(OH)D_3$ undergoes a secondary hydroxylation within the kidney to form the predominant active metabolite 1,25-hydroxycolecalciferol ($1,25(OH)_2D_3$, calcitriol). The metabolites circulate in the blood bound to a specific α-globin.

After a single oral dose of Colecalciferol, the maximum serum concentrations of the primary storage form are reached after approximately 7 days. $25(OH)D_3$ is then slowly eliminated with an apparent half-life in serum of about 50 days. Colecalciferol and its metabolites are excreted mainly in the bile and faeces.

After high doses of Colecalciferol, serum concentrations of $25(OH)D_3$ may be increased for months. Overdose-induced hypercalcaemia may persist for weeks (see 4.9 "Overdose").

5.3 Preclinical safety data

Colecalciferol is well known and established product and has been used in clinical practice for many years. No further specific toxicological hazard for humans is expected other than in chronic overdosage where hypercalcaemia could be seen.

Colecalciferol overdosage in animals has been shown to induce malformations in rats, mice and rabbits at doses significantly higher than the human dose. The malformations included skeletal defects, microcephaly and cardiac malformations.

At doses equivalent to those used therapeutically, Colecalciferol has no teratogenic activity.

Colecalciferol has no potential mutagenic or carcinogenic activity.

6. Pharmaceutical particulars

6.1 List of excipients

Prosolve SMCC
Croscarmellose Sodium
HPMC Hypromellose 5 Cp
Titanium Dioxide
PEG 6000

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store below 30 ° C.

6.5 Nature and contents of container

30 caplets in a plastic jar

6.6 Special precautions for disposal and other handling

No special requirements for disposal

7. APPLICANT/MANUFACTURER

Afrab Chem Limited
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