SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

InVita D3 50,000 IU soft capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 50,000 IU colecalciferol (equivalent to 1.25 mg vitamin D3)

Excipients with known effect:
Each capsule contains 0.082 mg Allura Red AC (E129).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Soft capsule

Red, oval-shaped, soft capsule. It contains a slightly yellow oily liquid. Each capsule has "50" printed in white ink. Capsule dimensions are 12.8mm x 8.5mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

The treatment of vitamin D3 deficiency.

4.2 Posology and method of administration

Posology

1 capsule contains 50,000 IU vitamin D3.

- Paediatric posology
  - Due to lack of clinical data, InVita D3 is not recommended.

- Pregnancy and breastfeeding
  - Due to lack of clinical data, InVita D3 is not recommended.

- Adults

  Higher doses may be required in certain situations, see below.

  - Treatment of vitamin D3 deficiency (<25 nmol/l) 50,000 IU/week (1 capsule) for 6-8 weeks, followed by maintenance therapy (1400-2000 IU/day may be required, such as 1 capsule per month; 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.)

- Certain populations are at high risk of Vitamin D3 deficiency, and may require higher doses and monitoring of serum 25(OH)D:
  - Institutionalised or hospitalised individuals
  - Dark skinned individuals
  - Individuals with limited effective sun exposure due to protective clothing or consistent use of sun screens
  - Obese individuals
  - Patients being evaluated for osteoporosis
  - Use of certain concomitant medications (eg, anticonvulsant medications, glucocorticoids)
  - Patients with malabsorption, including inflammatory bowel disease and coeliac disease
  - Those recently treated for Vitamin D3 deficiency, and requiring maintenance therapy.

Special populations

Renal impairment

InVita D3 should not be used in combination with calcium in patients with severe renal impairment.

Hepatic impairment

No posology adjustment is required in patients with hepatic impairment.

Method of administration

Oral – The capsules should be swallowed whole with water.
Patients should be advised to take InVita D3 preferably with a meal (see section 5.2 Pharmacokinetic properties - "Absorption").

4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients.
- Hypercalcaemia and/or hypercalciuria.
- Nephrolithiasis and/or nephrocalcinosis
- Serious renal impairment
- Hypervitaminosis D
- Pseudohypoparathyroidismas the vitamin D requirement may be reduced due to phases of normal vitamin D sensitivity, involving the risk of prolonged overdose. Better-regulatable vitamin D derivatives are available for this.
- Pregnancy
- Children and adolescents (under 18 years of age)

4.4 Special warnings and precautions for use

Vitamin D3 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.

Caution is required in patients receiving treatment for cardiovascular disease (see section 4.5 Interaction with other medicinal products and other forms of interaction - cardiac glycosides including digitalis).

InVita D3 should be prescribed with caution in patients with sarcoidosis, due to a possible increase in the metabolism of Vitamin D3 in its active form. In these patients the serum and urinary calcium levels should be monitored.

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.

Oral administration of high-dose Vitamin D3 (500,000 IU by single annual bolus) was reported to result in an increased risk of fractures in elderly subjects, with the greatest increase occurring during the first 3 months after dosing.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of anticonvulsants (such as phenytoin) or barbiturates (and possibly other drugs that induce hepatic enzymes) may reduce the effect of Vitamin D3 by metabolic inactivation.

In cases of treatment with thiazide diuretics, which decrease urinary elimination of calcium, monitoring of serum calcium concentration is recommended.

Concomitant use of glucocorticoids can decrease the effect of Vitamin D3.

In cases of treatment with drugs containing digitalis and other cardiac glycosides, the administration of Vitamin D3 may increase the risk of digitalis toxicity (arrhythmia). Strict medical supervision is needed, together with serum calcium concentration and electrocardiographic monitoring if necessary.

Simultaneous treatment with ion exchange resin such as cholestyramine, colestipol hydrochloride, orlistat or laxative such as paraffin oil may reduce the gastrointestinal absorption of Vitamin D3,.

The cytotoxic agent actinomycin and imidazole antifungal agents interfere with Vitamin D3 activity by inhibiting the conversion of 25-hydroxyVitamin D3 to 1,25-dihydroxyVitamin D3 by the kidney enzyme, 25-hydroxyVitamin D3-1-hydroxylase.

4.6 Fertility, pregnancy and lactation

In pregnancy and lactation the high strength formulation is not recommended and a low strength formulation should be used.

Pregnancy

There are no or limited amount of data from the use of colecalciferol in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3 Preclinical safety data). The recommended daily intake for pregnant women is 400 IU, however, in women who are considered to be Vitamin D3 deficient a higher dose may be required (up to 2000 IU/day- 10 drops with the oral drops presentation).
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 D3 and its metabolites are excreted in breast milk.

Breast-feeding

Vitamin D3 can be prescribed while the patient is breast-feeding if necessary. This supplementation does not replace the administration of Vitamin D3 in the neonate

Fertility

There is no data regarding treatment with vitaminD3 and its effects on fertility.

4.7 Effects on ability to drive and use machines

There are no data on the effects of InVita D3 on the ability to drive. However, an effect on this ability is unlikely.

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.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms of overdose

Ergocalciferol (vitamin D2) and colecalciferol (vitamin D3) have a relatively low therapeutic index. The threshold for vitamin D intoxication is between 40,000 and 100,000 IU daily for 1 to 2 months in adults with normal parathyroid function. Infants and small children may react sensitively to far lower concentrations. Therefore, it is warned against intake of vitamin D without medical supervision.
Overdose leads to increased serum and urinary phosphorus levels, as well as hypercalcaemic syndrome and consequently calcium deposits in the tissues and above all in the kidneys (nephrolithiasis, nephrocalcinosis) and the vessels.
Discontinue InVita D3 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.
Chronic overdosage may lead to vascular and organ calcification, as a result of hypercalcaemia.
The symptoms of intoxication are little characteristic and manifest as nausea, vomiting, initially also diarrhoea, later constipation, loss of appetite, weariness, headache, muscle pain, joint pain, muscle weakness, persistent sleepiness, azotaemia, polydipsia and polyuria and, in the final stage, dehydration. Typical biochemical findings include hypercalcaemia, hypercalciuria, as well as increased serum 25 hydroxy colecalciferol concentrations.

Treatment of overdose
Symptoms of chronic vitamin D overdosage may require forced diuresis as well as administration of glucocorticoids or calcitonin.
Overdosage requires measures for treating the - often persisting and under certain circumstances life- threatening - hypercalcaemia.
The first measure is to discontinue the vitamin D preparation; it takes several weeks to normalise hypercalcaemia caused by vitamin D intoxication.
Depending on the degree of hypercalcaemia, measures include a diet that is low in calcium or free of calcium, abundant liquid intake, increase of urinary excretion by means of the drug furosemide, as well as the administration of glucocorticoids and calcitonin.
If kidney function is adequate, calcium levels can be reliably lowered by infusions of isotonic sodium chloride solution (3–6 liters in 24 hours) with addition of furosemide and, in some circumstances, also 15 mg/kg body weight/hour sodium edetate accompanied by continuous calcium and ECG monitoring. In oligoanuria, in contrast, haemodialysis (calcium-free dialysate) is necessary.
No special antidote exists.

It is recommended to point out the symptoms of potential overdose to patients under chronic therapy with higher doses of vitamin D (nausea, vomiting, initially also diarrhoea, later constipation, anorexia, weariness, headache, muscle pain, joint pain, muscle weakness, persistent sleepiness, azotaemia, polydipsia and polyuria).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues, colecalciferol ATC

Code: A11CC05

In its biologically active form Vitamin D3 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 D3. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active Vitamin D3.

5.2 Pharmacokinetic properties

The pharmacokinetics of Vitamin D3 is well known.

Absorption

Vitamin D3 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 D3.

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 D3 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 D3 occurs in subjects with malabsorption.

Obese subjects are less able to maintain Vitamin D3 levels with sun exposure, and are likely to require larger oral doses of Vitamin D3 to replace deficits.

5.3 Preclinical safety data

Pre-clinical studies conducted in various animal species have demonstrated that toxic effects occur in animals at doses much higher than those required for therapeutic use in humans.

In toxicity studies at repeated doses, the effects most commonly reported were increased calciuria and decreased phosphaturia and proteinuria. Hypercalcaemia has been reported in high doses. In a state of prolonged hypercalcaemia, histological alterations (calcification) were more frequently borne by the kidneys, heart, aorta, testes, thymus and intestinal mucosa.

Colecalciferol has been shown to be teratogenic at high doses in animals.

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

all-rac-α-tocopherol (E307)
Medium Chain Triglycerides
Glycerol
Gelatine
Allura Red AC (E129)
Opacode® White imprinting ink

- Shellac (E904)
- Titanium dioxide (E171)
- Simethicone

6.2 Incompatibilities

Not applicable

6.3 Shelf life

30 months

6.4 Special precautions for storage

Do not store above 25°C.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

3 capsules packed in PVDC/Aluminium foil blisters, inserted into a cardboard carton.

6.6 Special precautions for disposal

Any unused product should be disposed of in accordance with the local requirements.

7 MARKETING AUTHORISATION HOLDER

Consilient Health Limited,

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Dublin 2, D02 Y754,

Ireland

8 MARKETING AUTHORISATION NUMBER(S)

PL 24837/0074

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21/07/2016

10 DATE OF REVISION OF THE TEXT

12/02/2024