SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

InVita D3 2,400 IU/ml oral drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution (36 drops) contains 0.06 mg colecalciferol, equivalent to 2,400 IU vitamin D3.

1 drop contains 1.67 microgram colecalciferol, equivalent to 67 IU vitamin D3.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Clear, slightly yellow, oily liquid with an orange odour

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Prevention of vitamin D deficiency in infants and children
- Prevention of vitamin D deficiency in pregnant and breast-feeding women

4.2 Posology and method of administration

Posology

1 drop contains 67 IU vitamin D3.

- Paediatric posology
  - prevention of deficiency 0-1 years 400 IU/day (6 drops)
  - prevention of deficiency 1-18 years 600 IU/day (9 drops)

- Pregnancy and breast-feeding posology
  - prevention of deficiency 400 IU/day (6 drops)

- Special populations
  - patients with renal impairment: no specific adjustment is required
  - Other conditions: in obese patients, patients with malabsorption syndromes, and patients on medications affecting vitamin D metabolism, higher doses are required for the prevention of vitamin D deficiency (2 - 3 times higher).

Method of administration

Patients should be advised to take InVita D3 preferably with a meal (see section 5.2 Pharmacokinetic properties - "Absorption").

The product should be shaken before use.

InVita D3 can be taken as is or to facilitate the intake it can also be mixed with a spoonful or a small amount of cold or lukewarm food immediately prior to use. The patient should be sure to take the entire dose.

In children, InVita D3 can be mixed with a small amount of children's foods, yogurt, milk, cheese or other dairy products. The parents should be warned not to mix InVita D3 into a bottle of milk or container of soft foods in case the child does not consume the whole portion, and does not receive the full dose. The parents should ensure that their child takes the entire dose. In children who are not breast-fed, the prescribed dose should be administered with a meal.

See also section 6.6, Special precautions for handling and disposal.

4.3 Contraindications

- Hypersensitivity to colecalciferol or to any of the excipients in the product.
- Hypercalcaemia and/or hypercalciuria.
- Hypervitaminosis D
- Kidney stones (nephrolithiasis, nephrocalcinosis) in patients with current chronic
- Hypercalcaemia

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.

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 D 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 D in cases associated with treatments already containing vitamin D, foods enriched with vitamin D, cases using milk enriched with vitamin D, and the patient's level of sun exposure.

There is no clear evidence for causation between vitamin D 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 D (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 D.

In cases of treatment with drugs containing digitalis and other cardiac glycosides, the administration of vitamin D 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 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

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 D deficient a higher dose may be required (up to 2 000 IU/day - 10 drops). 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.

Breast-feeding

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

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

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 authorisation 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 at: www.mhra.gov.uk/yellowcard.

4.9 Overdose

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. 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 InVita D3 and initiate rehydration.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vitamin D and analogues, colecalciferol

ATC Code: A11CC05

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. 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-colecalciferol and then undergoes further hydroxylation in the kidney to form the active metabolite 1, 25- dihydroxy colecalciferol (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

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 acetate
- Sweet orange peel oil
- Polyglyceryl oleate (E475)
- Olive oil, Refined

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

After first opening the bottle: the product may be stored for a maximum of 3 months.

6.4 Special precautions for storage

Store in the original package, in order to protect from light.

6.5 Nature and contents of container

1, 2, 3 or 4 dropper container(s) with 10 ml solution. Container: 10 ml molded glass bottles, brown, glass type III. Dropper: Central dropper made of polyethylene, white. Closure: Screw cap made of polypropylene, white.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Consilient Health Limited,

5th Floor, Beaux Lane House,

Mercer Street Lower,

Dublin 2,

Ireland

8 MARKETING AUTHORISATION NUMBER(S)

PL 24837/0046

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/01/2015

10 DATE OF REVISION OF THE TEXT

30/07/2015