Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Altavita D3 50,000IU oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution (1single-dose oral solution) contains 1.25 mg colecalciferol, equivalent to 50,000 IU vitamin D3.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution.

Clear, slightly yellow, oily liquid with an orange odour.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

The treatment of vitamin D deficiency.

4.2 Posology and method of administration

Posology

Paediatric posology:
Due to a lack of clinical data, altavitaD3 is not recommended.

Pregnancy and breastfeeding:
Due to a lack of clinical data, altavitaD3 is not recommended.

Adults:
Treatment of vitamin D deficiency (<25 nmol/l) 50,000 IU/week (1single-dose oral solution) for 6-8 weeks, followed by maintenance therapy (equivalent to 1400-2000 IU/day, such as 1 single-dose 50,000 IU oral solution 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).

Certain populations ar e at high risk of vita min D 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 (e.g., anticonvulsant medications, glucocorticoids)
- Patients with malabsorption, including inflammatory bowel disease and coeliac disease
- Those recently treated for vitamin D deficiency, and requiring maintenance therapy.

Special populations

Renal impairment
altavitaD3 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

Patients should be advised to take altavitaD3 preferably with meal (see section 5.2 Pharmacokinetic properties - "Absorption").

Administration to adults:
The single-dose oral solution should be either emptied into the mouth and swallowed orally, or emptied onto a spoon and taken orally. altavitaD3 can also be taken by mixing with a **small amount** of cold or lukewarm food/drink **immediately** to use.

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

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
- Pseudohypoparathyroidism as 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.

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).

altavitaD3 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 increases 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

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 D deficient a higher dose may be required (up to 2000 IU/day).

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.

Fertility
There is no data regarding treatment with vitamin D3 and its effects on fertility.

4.7 Effects on ability to drive and use machines

Not relevant.

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 react ions 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: HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

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 altavitaD3 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 hydroxycolecalciferol concentrations.

Treatment of over dose

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, 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 for m of vitamin D3. 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-dihydroxycolecalciferol (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

Tocopherol acetate
Polyglyceryl oleate (E475)
Olive oil,refined
Sweet orange peel oil.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Do not store above 30°C.

Do not freeze or refrigerate.

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

6.5 Nature and contents of container

Transparent PVC/PVDC/PE single-dose oral solutions

Original pack with 1, 2, 3, 4, 5 or 6 single dose oral solutions

Not all pack sizes may be marketed

6.6 Special precautions for disposal and other handling

No special requirements

Any unused product or waste materials 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

PA1876/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10th July 2015

10 DATE OF REVISION OF THE TEXT