SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

SoliCol D3 20,000 IU Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

20,000 IU of Colecalciferol BP (equivalent to 500 microgram of vitamin D3)

Excipient with known effect: Also contains sucrose (approximately 45mg per tablet).

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Tablet

Off-white to yellowish oval tablets debossed on one side with '4'.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- The prevention and treatment of vitamin D deficiency.
- As an adjunct to specific therapy for osteoporosis in patients with vitamin D deficiency or at risk of vitamin D insufficiency.

4.2 Posology and method of administration

Posology

Paediatric posology:

- Prevention of vitamin D deficiency 12-18 years: 20 000 IU (1 tablet) every 6 weeks
- Treatment of vitamin D deficiency 12 – 18 years: 20 000 IU (1 tablet) once every 2 weeks for 6 weeks

Adults:

- Prevention of vitamin D deficiency: 20 000 IU/month (1 tablet), higher doses may be required in certain situations, see below
- Treatment of vitamin D deficiency; 40 000 IU/week (2 tablets) for 7 weeks, followed by maintenance therapy (equivalent to 1400 – 2000 IU/day, such as 2-3 tablets 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 are at risk of vitamin 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.

SoliCol D3 20 000 IU Tablets should not be given to children under 12 years due to the risk of choking.

Infants and young children (0 – 12 years**)**

Not recommended for children under 12 years.

Pregnancy and breast feeding

SoliCol D3 20 000 IU Tablets are not recommended during pregnancy unless the clinical condition of the woman requires treatment.

Colecalciferol and its metabolites are excreted in breast milk. Overdose in infants induced by nursing mothers has not been observed but allowance for any maternal dose should be made when prescribing vitamin D products to a breast-fed child.

Method of administration

This medicine is taken orally.

The tablet should be swallowed whole with water, preferably with the main meal of the day.

4.3 Contraindications

Hypersensitivity to colecalciferol or to any of the excipients listed in section 6.1

Hypercalcaemia and/or hypercalciuria

Hypervitaminosis D

Severe renal impairment

Kidney stones (nephrolithiasis, nephrocalcinosis)

4.4 Special warnings and precautions for use

SoliCol D3 Tablets should not be given to infants and children under 12 years of age.

Medical supervision is required whilst on treatment to prevent hypercalcaemia.

Allowances should be made for vitamin D supplements from other sources (other vitamin D products, dietary sources and the patient's level of sun exposure) while accounting for the dose of vitamin D3 (cholecalciferol) necessary for treatment.

Dosage should be individualised.

Adequate fluid intake should be maintained.

All patients receiving pharmacological doses of vitamin D should have their plasma calcium concentration checked at regular intervals and whenever nausea and vomiting are present.

Vitamin D should be used with caution in patients with impaired renal function and those with renal calculi. 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. Calcium supplements should be given under close medical supervision and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should also be taken into account.

Caution should be exercised in patients with heart disease or arteriosclerosis who might be at increased risk of organ damage if hypercalcaemia were to occur and those who are receiving treatment for cardiovascular disease (see section 4.5 - Interaction with other medicinal products and other forms of interaction - cardiac glycosides including digitalis).

SoliCol D3 Tablets should be prescribed with caution in patients suffering from sarcoidosis because of the risk of increased metabolism of vitamin D to its active form. Serum and urinary calcium levels should be monitored in these patients.

Patients with rare hereditary problems of galactose intolerance, fructose intolerance, glucose-galactose malabsorption, the Lapp-lactase deficiency, or sucrase-isomaltase insufficiency should not take this medicine.

Oral administration of high-dose vitamin D (500,000 IU as a 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

Simultaneous treatment with ion exchange resins such as cholestyramine, colestipol hydrochloride and orlistat, or laxative such as paraffin oil, may reduce the gastrointestinal absorption of vitamin D.

Absorption of calcium may be reduced by oral sodium sulphate or parenteral magnesium sulphate.

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

Vitamin D requirements may be increased in patients taking anticonvulsants (e.g. carbamazepine, phenobarbital, phenytoin and primidone) as these drugs can reduce the effect of vitamin D because of metabolic activation.

The effects of digitalis and other cardiac glycosides may be accentuated with the oral administration of calcium combined with vitamin D. Strict medical supervision is needed during such treatment, and if necessary ECG and calcium should be monitored.

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 thiazide diuretics increases the risk of hypercalcaemia due to decreased urinary elimination of calcium. Serum calcium concentration should be monitored during such treatment.

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

4.6 Fertility, pregnancy and lactation

The recommended daily intake for pregnant and lactating women is 400 IU; however, a higher dose (up to 2000 IU/day) may be required in women who are considered to be vitamin D deficient. Because of lower level of requirement during pregnancy and lactation, high-strength vitamin D3 formulations such as SoliCol D3 20,000 IU Tablets are not appropriate for use during pregnancy and breast-feeding.

Pregnancy

There is inadequate data on the use of colecalciferol in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). 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.

Breast-feeding

Vitamin D and its metabolites are excreted in breast milk; however, overdose in infants induced by nursing mothers has not been observed. While 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

SoliCol D3 Tablets have no influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse events are generally associated with excessive intake of colecalciferol, leading to the development of hypercalcaemia. The symptoms of hypercalcaemia can include: anorexia, nausea, vomiting, diarrhoea, loss of weight, headache, polyuria,

thirst, vertigo, constipation, fatigue, bone pain, muscle weakness, abdominal pain, mental disturbances, impaired renal function, kidney stones, and cardiac arrhythmias.

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: Uncommon (≥1/1,000 to <1/100); Rare (≥1/10,000 to <1/1,000); or, Not Known (cannot be estimated from the available data).

Immune system disorders

Not known: Hypersensitivity reactions such as angioedema or laryngeal oedema.

Metabolism and nutrition disorders

Uncommon: Hypercalcaemia and hypercalciuria

Skin and subcutaneous tissue 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

An overdose manifests as hypercalcaemia and hypercalciuria, the symptoms of which include the following: anorexia, nausea, vomiting, constipation, dehydration, thirst, polyuria, polydipsia, weakness and apathy.

A single acute overdose is virtually non-toxic and requires supportive treatment with liberal fluids only.

Chronic administration to patients in excess of their daily requirement can cause hypercalcaemia, hypercalciuria and hyperphosphataemia. Chronic overdoses can lead to vascular and organ calcification as a result of hypercalcaemia. Concomitant high intake of calcium and phosphate may lead to similar abnormalities.

Treatment of chronic overdose with resulting hypercalcaemia consists of immediate withdrawal of the vitamin, a low calcium diet, and generous fluid intake. Severe cases may require hydration with intravenous saline together with symptomatic and supportive treatment as indicated by the patient's clinical condition. Plasma calcium and urea & electrolytes should be monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues - Colecalciferol

ATC Code: A11CC05

Vitamin D3 (cholecalciferol) is a steroid derivative which controls the calcification of bones in both the young and old. Administration of vitamin D3 counteracts development of rickets in children and osteomalacia in adults. In addition to bone and intestinal mucosa many other tissues have vitamin D receptors, to which the active hormonal form of vitamin D, calcitriol, binds.

Vitamin D increases the intestinal absorption of calcium and phosphate.

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 kidney, it inhibits the excretion of calcium and phosphate by promoting tubular resorption.

It also counteracts the increase of parathyroid hormone (PTH) which is caused by calcium deficiency and which causes increased bone resorption.

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.

Distribution and Biotransformation

Colecalciferol is hydroxylated in the liver to form 25-hydroxycolecalciferol and then undergoes further hydroxylation in the kidney to form the active metabolite 1,25 dihydroxycolecalciferol (calcitriol).

The metabolites circulate in the blood bound to a specific α–globulin.

Elimination

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 to that in 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

Vitamin D is a well known compound that has been widely used in clinical practice for many years. Colecalciferol has a high therapeutic index and hence toxicity is only likely to occur in chronic overdosage where hypercalcaemia could result.

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.

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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

DL-alpha tocopherol

Modified food starch

Medium-chain triglycerides

Sodium ascorbate crystalline

Silicon dioxide

Sucrose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

12 months.

6.4 Special precautions for storage

Store below 25°C.

Keep the blister in the outer carton in order to protect from light.

6.5 Nature and contents of container

Tablets are packed in blisters composed of clear PVC/Aclar polymer film and tempered aluminium foil. Each pack contains 30 tablets.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 43196/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

18/12/2015

10 DATE OF REVISION OF THE TEXT

28/09/2018