SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

STRIVIT-D3 800 IU Capsules, Soft

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 800 IU colecalciferol (equivalent to 20 micrograms vitamin D_3).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule, soft (capsule)

Translucent blue capsule (size 2) with no markings.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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.

Colecalciferol is indicated in adults, the elderly and adolescents.

4.2 Posology and method of administration

Posology

Adults
Vitamin D deficiency
For vitamin D deficiency in adults and the elderly (serum levels <25 nmol/l (<10 ng/ml)), 1-4 capsules (800-3200 IU) daily for up to 12 weeks dependent upon the severity of the disease and the patient's response to treatment.

Vitamin D insufficiency
For vitamin D insufficiency in adults and the elderly (serum levels 25 – 50 nmol/l (10-20 ng/mL)), long term maintenance therapy following treatment of deficiency in adults and the elderly and prevention of vitamin D deficiency, 1-2 Capsules (800-1600 IU) daily.

Osteoporosis
As an adjunct to specific therapy for osteoporosis, 1 capsule daily.

Paediatric population
Vitamin D deficiency or insufficiency
Vitamin D deficiency or insufficiency in children over 12 years – 1 capsule daily depending on the severity of the disease and the patient's response to treatment. Should only be given under medical supervision.
Colecalciferol should not be used in children under 12 years.

Dosage in hepatic impairment
No dose adjustment is required

Dosage in renal impairment
Colecalciferol should not be used in patients with severe renal impairment (see section 4.3).

Method of administration

Oral.

The capsules should be swallowed whole (not chewed) with water.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Hypervitaminosis D
- Calcium nephrolithiasis, nephrocalcinosis
- Diseases or conditions resulting in hypercalcaemia and/or hypercalciuria
- Severe renal impairment

4.4 Special warnings and precautions for use

In the case of therapeutic treatment the dose should be established on an individual basis for the patients by regular checking of plasma calcium levels. During long-term treatment, serum calcium level, urinary calcium excretion and renal function should be monitored by measuring the serum creatinine level. Monitoring is especially important for elderly patients who concomitantly take cardiac glycosides or diuretics (see section 4.5), and in the case of hyperphosphataemia, as well as for patients with an increased risk of lithiasis. In case of hypercalciuria (exceeding 300 mg (7.5 mmol)/24 hours) or signs of impaired renal function the dose should be reduced or the treatment discontinued.

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. 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 (see section 4.3, Contraindications). Similar monitoring is necessary for children whose mother receives treatment with vitamin D in pharmacological amounts. Some children may react with increased sensitivity to the effect of vitamin D.

Vitamin D3 capsules should not be taken if pseudohypoparathyroidism is present (the need for vitamin D may be reduced by the sometimes normal sensitivity to vitamin D, with a risk of long term overdose). In such cases, more manageable vitamin D derivatives are available.

Caution is required in patients receiving treatment for cardiovascular disease (see Section 4.5 – cardiac glycosides including digitalis).

Colecalciferol 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 from other sources. The concomitant use of multivitamin products and dietary supplements containing vitamin D should be avoided.

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
Colecalciferol should not be given to children under 12 years.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use with calcium containing products administered in large doses may increase the risk of hypercalcaemia. Thiazide diuretics reduce the urinary excretion of calcium. Due to the increased risk of hypercalcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics or with calcium containing products taken in large doses.

Concomitant treatment with anticonvulsants (like phenytoin), hydantoin or barbiturates can decrease the effect of vitamin D because of metabolic activation. Concomitant use of glucocorticoids can decrease the effect of vitamin D. Systematic corticosteroids inhibit the absorption of calcium. Long-term use of corticosteroids may offset the effect of vitamin D.

Products containing magnesium (like antacids) may not be taken during vitamin D treatment because of the risk of hypermagnesaemia.

Concomitant use of calcitonin, etidronate, gallium nitrate, pamidronate or plicamycin with vitamin D may antagonise the effect of these products in hypercalcaemia treatment.

Products containing phosphor used in large doses, given concomitantly may increase the risk of hyperphosphataemia.

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 and, if necessary monitoring of ECG and calcium.

Simultaneous treatment with ion exchange resins such as cholestyramine or laxatives 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). 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). In patients without a vitamin D deficiency, the daily vitamin D intake during pregnancy may not exceed 600 IU. Colecalciferol can be used up to 2,000 IU/day only in case of a Vitamin D 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. In pregnant women, overdosage of vitamin D3 should be avoided, since prolonged hypercalcaemia has been sometimes associated with retardation of physical and mental development, supravalvular aortic stenosis and retinopathy in the child.

Breast-feeding
Vitamin D 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.

Fertility
There are no data on the effect of colecalciferol on fertility. However, normal endogenous levels of vitamin D are not expected to have any adverse effects on fertility.

4.7 Effects on ability to drive and use machines

Colecalciferol has no or negligible influence on the ability to drive and use machines.

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).

Immune system disorders
Not known (cannot be estimated from the available data): hypersensitivity reactions such as angio-oedema or laryngeal oedema.

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 Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The most serious consequence of acute or chronic overdose is hypervitaminosis, hypercalcaemia and hyperphosphatemia due to vitamin D toxicity. Symptoms may include nausea, vomiting, polyuria, anorexia, weakness, apathy, thirst, constipation, abdominal pain, muscle weakness, confusion, polydipsia, bone pain, calcification in the kidneys, kidney stones, vertigo, and cardiac arrhythmia in severe cases. Chronic overdoses can lead to vascular and organ calcification as a result of hypercalcaemia. Hypercalcaemia in extreme cases may lead to coma or even death. Persistently high levels of calcium may cause irreversible renal impairment and soft tissue calcification.

Treatment should consist of stopping all intake of vitamin D. At the same time, the use of thiazide diuretics, lithium, vitamin D and A as well as cardiac glycosides should also be discontinued. In the case of patients with impaired consciousness gastric emptying is also necessary. Rehydration and mono- or combined therapy with loop diuretics, bisphosphonates, calcitonin and corticosteroids may be used depending on the severity of the overdose. Serum electrolyte levels, renal function and diuresis should be monitored. In severe cases ECG and central venous pressure monitoring may be necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues, ATC code: A11CC05

Mechanism of action
In its biologically active form vitamin D_3 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_3. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active vitamin D_3.

Vitamin D receptors are present in several other tissues besides the skeletal system, therefore vitamin D has diverse effect in several physiological processes. As for its cellular biological effects, study data are available for the autocrine/paracrine realization of growth and differentiation control on hematopoietic and immune cells, skin-, skeletal- and smooth muscle cells, as well as on the cells of the brain, liver and certain endocrine organs.

Vitamin D, through its effect of increasing calcium absorption very effectively increases the bone resorption decreasing effect of calcium. In a study with 148 elderly, postmenopausal women, concomitant administration of 800 IU vitamin D (colecalciferol) and 1200 mg. calcium resulted in 72% increase in 25(OH)D level and 17% decrease in PTH level as compared to supplementation with calcium alone.

5.2 Pharmacokinetic properties

Absorption
The pharmacokinetics of vitamin D is well known. Vitamin D is well absorbed from the gastro-intestinal tract in the presence of bile.

Distribution and biotransformation
It 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 - globin.

Elimination
Vitamin D and its metabolites are excreted mainly in the bile and faeces.

5.3 Preclinical safety data

Colecalciferol has been shown to be teratogenic in high doses in animals (4-15 times the human dose). Offspring from pregnant rabbits treated with high doses of vitamin D had lesions anatomically similar to those of supravalvular aortic stenosis and offspring not showing such changes show vasculotoxicity similar to that of adults following acute vitamin D toxicity. There is no further information of relevance to the safety assessment in addition to what is stated in other parts of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content
Maize oil, refined

Capsule shell
Gelatin
Glycerol (E 422)
Brilliant Blue Supra containing brilliant blue for coloring of food (E 133), sodium chloride and sodium sulphate
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions. Keep the blister in the outer carton in order to protect from light.

6.5 Nature and contents of container

Coated PVC film with aluminum blister foil packed in cartons.

Pack sizes: 28, 30, 56, 60 and 90 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

Strides Arcolab International Ltd.
Unit 4, Metro Centre, Tolpits Lane
Watford, Hertfordshire WD 189SS
United Kingdom

8. MARKETING AUTHORISATION NUMBER(s)

PL 28176/0170

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

07/01/2016

10. DATE OF REVISION OF THE TEXT

17/07/2018