

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Solferol 10,000 IU Soft Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

10,000 IU Colecalciferol (equivalent to 250 micrograms Vitamin D3)

Excipients with known effect:

Each capsule also contains 16.5 milligrams of sorbitol and 45 micrograms of sunset yellow.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, soft (Capsule)

Orange coloured clear transparent round shaped gelatin capsule with a clear, colourless liquid fill.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of Vitamin D deficiency.

Prevention of Vitamin D deficiency in high-risk patients.

As an adjunct to specific therapy for osteoporosis in patients with Vitamin D deficiency or at risk of Vitamin D insufficiency.

Solferol Capsules is indicated in adults, the elderly and adolescents.

4.2 Posology and method of administration

Posology

Adults

Dose should be established on an individual basis depending on the extent of the necessary vitamin D supplementation. Vitamin D₃ 800 IU and 1,000 IU capsules are suitable for daily vitamin D supplementation while the 10,000 IU dose is suitable for weekly vitamin D dosing (equivalent to 1, 400 IU/day) respectively, which should be taken into consideration and dosage should be established by a physician.

Osteoporosis: For the adjunct therapy of osteoporosis a daily dose of 800-1,000 IU. A daily doses equivalent of 2,000 IU vitamin D should be considered in fragile elderly patients who are at particular risk of falls and fractures. Patients should receive supplemental calcium if intake from diet is inadequate.

Vitamin D deficiency (serum levels < 25 nmol/l or < 10 ng/ml) in adults and the elderly: 800 IU-4,000 IU daily for up to 12 weeks depending upon the severity of the disease and the patient's response to treatment.

Vitamin D insufficiency (serum levels 25-50 nmol/l or 10-20 ng/ml) in adults and the elderly:

AND

Long term maintenance therapy following treatment of deficiency in adults and the elderly:

AND

Prevention of vitamin D deficiency:

800-1600 IU daily.

Vitamin D deficiency or insufficiency in adolescents 12-18 years: 800 IU daily depending on the severity of the disease and the patient's response to treatment. Should only be given under medical supervision.

Hepatic impairment: no dose adjustment is necessary for patients with hepatic impairment.

During vitamin D therapy, calcium and phosphor intake has fundamental significance with respect to the success of the treatment.

Before starting the vitamin D therapy, the patient's dietary habits should be carefully evaluated by the doctor and artificially added vitamin D content of certain food types should be taken into consideration.

Certain populations are at high 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.

Medical supervision is required as dose response may vary dependent on patient response (see section 4.4).

Paediatric population

Solferol Capsules should not be used in children under 12 years.

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.
- Diseases/conditions associated hypercalcaemia and / or hypercalciuria.
- Calcium nephrolithiasis, nephrocalcinosis, D- hypervitaminosis
- 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 impaired renal function. In this case monitoring of calcium and phosphate levels is necessary, and the risk of soft tissue calcification should be taken into consideration. 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. Similar monitoring is necessary for children whose mother receive treatment with vitamin D in pharmacological amounts. Some children may react with increased sensitivity to the effect of vitamin D.

Solferol 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.

Solferol Capsules should be used with caution in patients with sarcoidosis because of the risk of vitamin D's increased transformation to its active form. Blood and urine calcium levels should be regularly monitored in these patients.

In the case of concomitant use with other medicinal product containing vitamin D, its vitamin D content should be taken into consideration. The concomitant use of multivitamin products and dietary supplements containing vitamin D should be avoided.

Medicinal products having effect through the inhibition of bone resorption decrease the calcium amounts derived from bone. In order to avoid this, as well as concomitantly to treatment with medicines enhancing bone development, it is necessary to take vitamin D and ensure proper calcium levels.

Paediatric population

Solferol Capsules are not indicated for use in children under 12 years.

This product contains sorbitol liquid partially dehydrated. The additive effect of concomitantly administered products containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.

The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.

Patients with rare hereditary problems of fructose intolerance should not take this medicine.

This product contains sunset yellow which may cause allergic reactions.

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 excretion of calcium with urine. Regular monitoring of the serum calcium level is necessary in the case of concomitant use with thiazide diuretics or with calcium containing products taken in large doses because of the increased risk of hypercalcaemia.

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.

Systematic corticosteroids inhibit the absorption of calcium. Long-term use of corticosteroids may offset the effect of vitamin D.

Simultaneous treatment with ion exchange resins (e.g. colestyramine), or laxatives (like paraffin oil) may impair the absorption of vitamin D.

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

Anticonvulsants, hydantoin, barbiturates or primidone may reduce the effect of vitamin D due to the activation of the microsomal enzyme system.

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.

4.6 Fertility, pregnancy and lactation

Pregnancy

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). In patients without a vitamin D deficiency, the daily vitamin D intake during pregnancy may not exceed 600 IU.

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. Overdoses of vitamin D have been shown to have teratogenic effects in animal experiments (See section 5.3). In pregnant women, overdosage of vitamin D₃ should be avoided, since prolonged hypercalcaemia has been sometimes associated with retardation of physical and mental development, supravulvar aortic stenosis and retinopathy in the child.

Breastfeeding

Solferol Capsules can be used during breastfeeding. Vitamin D and its metabolites pass into breast-milk. This should be considered when giving additional vitamin D to the child.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

The frequency of possible side effects listed below are defined as:

Very common ($\geq 1/10$)

Common ($\geq 1/100$ to $<1/10$)

Uncommon ($\geq 1/1,000$ to $<1/100$)

Rare ($\geq 1/10,000$ to $<1/1,000$)

Very rare ($<1/10,000$)

Not known (cannot be estimated from the available data)

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 the national reporting system.

HPRA Pharmacovigilance

Website: www.hpra.ie.

4.9 Overdose

Overdose of the product may cause hypervitaminosis, hypercalcaemia and hyperphosphatemia. Symptoms of hypercalcaemia: anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, confusion, polydipsia, polyuria, bone pain, calcification in the kidneys, kidney stones, vertigo, and cardiac arrhythmia in severe cases. 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 of hypercalcaemia: treatment with vitamin D (and calcium) should be discontinued. 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

Vitamin D increases the intestinal absorption of calcium, increases the calcium reabsorption in the kidneys and bone formation, and decreases the level of parathyroid hormone (PTH). 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.

Doses lower than the 800 IU dose of previous recommendations are sufficient for the maintenance of the ideal vitamin D supplementation but not sufficient for the treatment of vitamin D deficiency. The vitamin D supplementation required in the treatment of osteoporosis should be differentiated from the treatment of vitamin D deficiency and from therapeutic doses of vitamin D monotherapy.

The once-a-week administration of the weekly total dose results in the same effect daily administration because of the pharmacokinetic parameters of vitamin D. However, most experience from randomised controlled trials comes from daily dosages.

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 (colecalfiferol) 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.

A clinical study performed with vitamin D deficient patients treated in hospital showed that daily supplementation with 100 mg calcium and 800 IU vitamin D over 6 months has normalised plasma levels of the 25-hydroxylised metabolite of vitamin D, mitigated secondary hyperparathyreosis and decreased alkaline phosphatase levels.

In the case of muscle weakness or decreased muscle mass (for example in the elderly or patients with stroke) supplementation of vitamin D with the 800 IU dose (or higher) has a clearly demonstrated effect on muscle strength: it reduced the number of falls and had a beneficial effect on muscle mass. In another clinical trial the results demonstrated that a concomitant administration of vitamin D and calcium-citrate decreases the risk of falling due to muscle weakness in the elderly. In a 3-year placebo-controlled, double-blind study performed with the participation of 445 patients over 65 years of age, the participants received calcium citrate malate corresponding to 700 IU vitamin D /day and 500 mg elemental calcium /day resulting in significant decrease (46%) of the risk of falling (OR 0,54; 95% CI, 0,30-0,97) among treated women.

5.2 Pharmacokinetic properties

Absorption

Fat-soluble vitamin D3 is absorbed through the small intestine in the presence of bile acids with the help of micellum and gets into the blood through lymphatic circulation.

Distribution

Following absorption, vitamin D3 enters the blood as part of chylomicrons. Vitamin D3 is rapidly distributed mostly to the liver where it undergoes metabolism to 25-hydroxyvitamin D3, the major storage form. Lesser amounts are distributed to adipose and muscle tissue and stored as vitamin D3 at these sites for later release into the circulation. Circulating vitamin D3 is bound to vitamin D-binding protein.

Biotransformation

Vitamin D3 is rapidly metabolized by hydroxylation in the liver to 25-hydroxyvitamin D3, and subsequently metabolized in the kidney to 1,25-dihydroxyvitamin D3, which represents the biologically active form. Further hydroxylation occurs prior to elimination. A small percentage of vitamin D3 undergoes glucuronidation prior to elimination.

Elimination

Vitamin D and its metabolites are excreted in faeces and urine.

5.3 Preclinical safety data

At doses far higher than the human therapeutic range teratogenicity has been observed in animal studies. 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:

Medium chain triglycerides
Vitamin E Acetate (α -Tocopheryl Acetate)

Capsule Shell:
Gelatin
Glycerol (E422)
Sorbitol liquid partially dehydrated (E420)
Sunset Yellow (E110)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Aluminium PVCPVDC Blisters:
36 months

HDPE Containers and Amber Glass Bottles:
30 months

HDPE Containers and Amber Glass Bottles: Once opened use within 105 days.

6.4 Special precautions for storage

Store below 30°C.

6.5 Nature and contents of container

HDPE Containers
Amber Glass Bottles
Aluminium PVCPVDC Blisters
Pack sizes: 20 capsules/30 capsules/50 capsules/60 capsules/90 capsules
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Windzor Pharma Ireland Limited
The Office Suite
Unit 2 Holywell Commercial Centre
Swords
Co Dublin
Ireland

8 MARKETING AUTHORISATION NUMBER

PA23126/001/004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 6th October 2017
Date of last renewal: 21st June 2022

10 DATE OF REVISION OF THE TEXT

May 2022