Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Thorens 25 000 I.U. capsules, hard

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One capsule contains 625 micrograms colecalciferol (vitamin D3) equivalent to 25 000 IU.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Capsule, hard.

Hard gelatin capsule filled with oily solution. Transparent body and white cap, with a green band.
Capsule dimensions are 15.9 mm x 5.8 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Initial treatment of clinically relevant vitamin D deficiency in adults.

4.2 Posology and method of administration

Posology
The dosage must be determined individually by the treating doctor depending on the extent of the necessary vitamin D supplementation. The dose should be adjusted dependent upon desirable serum levels of 25-hydroxycolecalciferol (25(OH)D), severity of the disease and patients response to treatment.

Recommended dose:
25 000 IU every week.
After first month, lower doses may be considered.

Following this initial treatment, maintenance therapy may be required with a dose determined individually by the treating doctor.
Alternatively, national posologyrecommendations in treatment of vitamin D deficiency can be followed.

Special populations

Renal impairment
THORENS must not be used in patients with severe renal impairment.

Hepatic impairment
No posology adjustment is required in patients with hepatic impairment.

Paediatric population
THORENS 25 000 IU capsules is not recommended in children and adolescents under 18 years of age.

Pregnancy and breastfeeding
THORENS 25 000 IU capsules is not recommended.

Method of administration
The capsules should be swallowed whole.
Patients should be advised to take THORENS preferably with a meal (see section 5.2 Pharmacokinetic properties - "Absorption").

4.3 Contraindications

Hypersensitivity to the active ingredient, colecalciferol (vitamin D_3), or to any of the excipients listed in section 6.1.
Hypercalcaemia, hypercalciuria.
Hypervitaminosis D.
Kidney stones (nephrolithiasis, nephrocalcinosis) in patients with current chronic hypercalcaemia.
Severe renal impairment.

4.4 Special warnings and precautions for use

Vitamin D_3 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 have to be used.

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).

THORENS must be used with particular caution in patients treated with benzothiadiazine derivatives (see section 4.5 Interaction with other medicinal products and other forms of interaction) and in immobilized patients (risk of hypercalcaemia and hypercalciuria). Plasma and urinary calcium levels should be monitored in these patients.

THORENS should be prescribed with caution in patients with sarcoidosis, due to a possible increase in the metabolism of vitamin D_3 in its active form. In these patients the serum and urinary calcium levels should be monitored.

THORENS 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."

Allowances should be made for the total dose of vitamin D_3 in cases associated with treatments already containing vitamin D, foods enriched with vitamin D_3, 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_3 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.

During long-term treatment with a daily dose exceeding 1,000 IU vitamin D_3 the serum calcium values must be monitored.

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 D_3 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_3.

In cases of treatment with drugs containing digitalis and other cardiac glycosides, the administration of vitamin D_3 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_3.

The cytotoxic agent actinomycin and imidazole antifungal agents interfere with vitamin D_3 activity by inhibiting the conversion of 25-hydroxyvitamin D_3 to 1,25-dihydroxyvitamin D_3 by the kidney enzyme, 25-hydroxyvitamin D-1-hydroxylase.

Rifampicin may reduce the effectiveness of colecalciferol due to hepatic enzyme induction.

Isoniazid may reduce the effectiveness of colecalciferol due to inhibition of the metabolic activation of colecalciferol.

4.6 Fertility, pregnancy and lactation

THORENS 25 000 IU capsules is not recommended in pregnancy and lactation. A low strength formulation should be used.

Pregnancy
There are no or limited amount of data from the use of colecalciferol (vitamin D_3) in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3 Preclinical safety data). Long-term overdose must be avoided during pregnancy, since the resulting protracted hypercalcaemia may lead to physical and mental retardation, supravalvular aortic stenosis and retinopathy in the child. The recommended daily intake for pregnant women is 400 IU, however, in women who are considered to be vitamin D_3 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. Treatment of pregnant women with high-dose vitamin D is not recommended.

Breast-feeding
Vitamin D_3 and its metabolites are excreted in breast milk. Vitamin D_3 can be prescribed while the patient is breast-feeding if necessary. This supplementation does not replace the administration of vitamin D_3 in the neonate.

Overdose in infants induced by nursing mothers has not been observed, however, when prescribing additional vitamin D_3 to a breast-fed child the practitioner should consider the dose of any additional vitamin D_3 given to the mother. Treatment with high-dose vitamin D in breast-feeding women is not recommended.

Fertility
There are no data on the effect of THORENS 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

There are no data on the effects of THORENS 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 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

Discontinue THORENS 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 THORENS and initiate rehydration.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vitamin D_3 and analogues, colecalciferol
ATC Code: A11CC05

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.

5.2 Pharmacokinetic properties

The pharmacokinetics of vitamin D_3 is well known.

Absorption
Vitamin D_3 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_3.

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_3 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_3 occurs in subjects with malabsorption.

Obese subjects are less able to maintain vitamin D_3 levels with sun exposure and are likely to require larger oral doses of vitamin D_3 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 (vitamin D_3) has been shown to be teratogenic at high doses in animals.

At doses equivalent to those used therapeutically, colecalciferol (vitamin D_3) has no teratogenic activity.

Colecalciferol (vitamin D_3) has no potential mutagenic or carcinogenic activity.

Microcephaly, cardiac malformations and skeletal abnormalities were observed in the offspring. Offspring from pregnant rabbits treated with high doses of vitamin D had lesions anatomically similar to supravalvular aortic stenosis and offspring not showing such changes show vasculotoxicity similar to that of adults following acute vitamin D toxicity. Colecalciferol is also foetotoxic in mice with fewer and smaller offspring from pregnant mice receiving medium and high dose Vitamin D.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Refined olive oil,
Gelatine,
Titanium dioxide (E 171),
Iron oxide yellow (E 172),
Iron oxide black (E 172).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 30° C.

Do not freeze.

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

6.5 Nature and contents of container

The immediate container is an Aluminium-PVC/PVDC blisters in cardboard boxes.

Packs of 3 capsules (1 blister/box), 4 capsules (1 blister/box), 8 capsules (2 blisters/box), 12 capsules (3 blisters/box) and 40 capsules (4 blisters/box).

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 the local requirements.

7 MARKETING AUTHORISATION HOLDER

Galen Pharma Ireland Limited
Finnabair Industrial Estate
Dundalk
Louth
A91P9KD
Ireland

8 MARKETING AUTHORISATION NUMBER

PA22680/005/003

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28th June 2019
Date of last renewal 11th March 2024

10 DATE OF REVISION OF THE TEXT

March 2024