SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fultium 20 000 IU Capsule

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:
Cholecalciferol (vitamin D_3, equivalent to 20 000 IU) 500 micrograms.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule, soft

Yellow coloured translucent soft gelatin capsule, 10.6 mm x 6.2 mm

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Initial treatment of symptomatic vitamin D deficiency in adults.

4.2 Posology and method of administration

Posology

Recommended dose: One capsule (20 000 IU) weekly.
After first month, lower doses may be considered, dependent upon desirable serum levels of 25-hydroxycolecalciferol (25(OH)D), the severity of the disease and the patient´s response to treatment.

Alternatively, national posology recommendations in treatment of vitamin D deficiency can be followed.

Dosage in hepatic impairment
No dose adjustment is required.

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

Paediatric population
Fultium is not recommended.

Method of administration

This medicine is taken orally.
The capsule should be swallowed whole with water, preferably with the main meal of the day.

4.3 Contraindications

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

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. In patients with severe renal insufficiency, vitamin D in the form of cholecalciferol may not be metabolised normally, Fultium is contraindicated (see section 4.3).

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

Fultium should not be taken if there is a tendency for the formation of calcium-containing kidney stones.

Fultium should be used with special caution in patients with impaired renal calcium and phosphate excretion, in treatment with benzothiadiazine derivatives and in immobilised patients (risk of hypercalcaemia, hypercalciuria). In these patients, plasma and urine calcium levels should be monitored.

Vitamin D_3 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.

Fultium should not be taken in case of 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.

During long-term treatment with an equivalent daily dose exceeding 1,000 IU vitamin D the serum calcium values and renal function must be monitored, especially in elderly patients. In case of hypercalcaemia or hypercalciuria (exceeding 300 mg (7.5 mmol)/24 hours) treatment has to be discontinued. If there are signs of impaired renal function, the dose should be reduced or the treatment discontinued.

The content of vitamin D in Fultium should be considered when prescribing other medicinal products containing vitamin D, analogues and metabolites of vitamin D and also when food and food supplements containing vitamin D are taken concomitantly. Additional doses of vitamin D and calcium should be taken under close medical supervision. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.

Paediatric population
Fultium is not recommended in children and adolescents under 18 years of age. Capsules are not a suitable dose form for children under 12 years, due to the risk of choking.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with phenytoin, isoniazid or barbiturates can decrease the effect of vitamin D because of metabolic activation. Concomitant use of glucocorticoids can decrease the effect of vitamin D.

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.

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

Simultaneous administration of benzothiadiazine derivates (thiazide diuretics) increase the risk of hypercalcaemia due to the reduction in renal calcium excretion. Plasma and urinary calcium levels should therefore be monitored.

Simultaneous treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil and with orlistat 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.

Ketoconazole may inhibit both synthetic and catabolic enzymes of vitamin D. Reductions in serum endogenous vitamin D concentrations have been observed following the administration of 300 mg/day to 1,200 mg/day ketoconazole for a week to healthy men. However, in vivo drug interaction studies of ketoconazole with vitamin D have not been investigated.

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
Vitamin D deficiency is harmful for mother and child. High doses of vitamin D have been shown to have teratogenic effects in animal experiments (see section 5.3). Overdose of vitamin D must be avoided during pregnancy, as prolonged hypercalcaemia can lead to physical and mental retardation, supravalvular aortic stenosis and retinopathy of the child.

Where there is a vitamin D deficiency the recommended dose is dependent on national guidelines, however, the maximum dose should not exceed 4,000 IU/day. Treatment of pregnant women with high-dose vitamin D is not recommended.

Breast-feeding
Vitamin D_3 and metabolites pass into the breast-milk. This should, however, be borne in mind when administering additional vitamin D to the child. Treatment with high-dose vitamin D in breast-feeding women is not recommended.

Fertility
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 about the effect of this product on driving capacity. An effect is, however, 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 the national reporting system listed in Appendix V.

4.9 Overdose

The most serious consequence of acute or chronic overdose is hypercalcaemia due to vitamin D toxicity. Symptoms may include nausea, vomiting, polyuria, anorexia, weakness, apathy, thirst and constipation. Chronic overdoses can lead to vascular and organ calcification as a result of hypercalcaemia.

Treatment should consist of stopping all intake of vitamin D and rehydration.

In severe cases haemodialysis (with calcium-free dialysate) may be required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues, 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

Absorption
Vitamin D is well absorbed from the gastro-intestinal tract in the presence of bile, so the administration with food might therefore facilitate the absorption of vitamin D_3.

Distribution and Biotransformation
Colecalciferol and its metabolites circulate in the blood bound to a specific globulin. 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), responsible for increasing calcium absorption. Vitamin D, which is not metabolised, is stored in adipose and muscle tissues.

After a single oral dose of colecalciferol, the maximum serum concentrations of the primary storage form are reached after approximately 7 days. 25-hydroxycolecalciferol is then slowly eliminated with an apparent half-life in serum of about 50 days.

Elimination
Vitamin D_3 and its metabolites are excreted mainly in the bile and faeces with a small percentage found in urine.

Special population
A defect in the metabolism and excretion of vitamin D has been described in patients with chronic renal failure.

5.3 Preclinical safety data

Effects in non-clinical single and repeat-dose toxicity studies were observed only at exposures of high doses. At very high doses teratogenicity was observed in animal studies. Normal endogenous levels of cholecalciferol has no potential mutagenic activity (negative in Ames-test). Tests on carcinogenicity activity have not been conducted.
There is no further information of relevance to the safety assessment in addition to what is stated in other parts of the SmPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content:
Maize oil, refined
Butylated hydroxytoluene (BHT) (E321)

Capsule shell:
Glycerol (E422)
Purified Water
Quinoline Yellow (E104)
Gelatin (E441)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.
Store blister foil in original container in order to protect from light.

6.5 Nature and contents of container

Opaque, white PVC/PVdC blister tray with aluminium foil.

Pack sizes: 4, 6, 15 or 50 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

[To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: {DD month YYYY}

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2022-01-20