SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Fultium 10 000 IU/ml Oral Drops, solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml oral solution contains:
Cholecalciferol (vitamin D_3, equivalent to 10 000 IU) 250 micrograms.

1 drop contains:
Cholecalciferol (vitamin D_3, equivalent to 250 IU) 6.25 micrograms.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral drops, solution

Pale yellow transparent, odourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Prevention and treatment of vitamin D deficiency in adults, adolescents and children with an identified risk.

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

Adults
Prevention of vitamin D deficiency and osteoporosis:
Recommended dose is 2-3 drops (500 IU- 750 IU) per day.

Treatment of vitamin D deficiency:
3 drops (750 IU) per day. Higher doses should be adjusted dependent upon desirable serum levels of 25-hydroxycolecalciferol (25(OH)D), the severity of the disease and the patient´s response to treatment.
The daily dose should not exceed 4,000 IU (16 drops per day).

Paediatric population
Prevention:
For prevention in adolescents (12 years to 18 years old) with an identified risk, the recommended dose is 2-3 drops (500 IU- 750 IU) per day. For children below 12 years, recommended doses may not be feasible to administer with this drop strength.

Treatment of deficiency in children and adolescents:

The dose should be adjusted dependent upon desirable serum levels of 25-hydroxycolecalciferol (25(OH)D), the severity of the disease and the patient´s response to treatment.
The daily dose should not exceed 1000 IU per day for infants <1 years, 2000 IU per day for children 1-10 years and 4000 IU per day for adolescents >11 years.

Alternatively, national posology recommendations in prevention and 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).

Method of administration
Oral

Fultium Drops can be dispensed onto a spoon or mixed with a small amount of cold or lukewarm food or drink immediately prior to use. The whole portion should be consumed.

For detailed instructions on administration of the medicinal product, see section 6.6.

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.

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

During pregnancy and breast-feeding adequate vitamin D intake is necessary. The recommended daily intake level for vitamin D during pregnancy and lactation follows national/European guidelines and is around 600 IU.

Pregnancy

Daily doses above 600 IU should be taken only when strictly indicated and only as it is absolutely necessary to correct vitamin D deficiency. During pregnancy, the daily intake should not exceed 4.000 IU vitamin D. 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. There are no indications that vitamin D at therapeutic doses is teratogenic in humans. Studies in animals have shown reproductive toxicity of high doses of vitamin D (see section 5.3).

Breast-feeding

Fultium can be used during breast-feeding in case of a vitamin D deficiency. Vitamin D and its metabolites pass into breast milk. This should be considered when giving additional vitamin D to the child.

Fertility
Normal endogenous levels of vitamin D are not expected to have any adverse effects on fertility. The impact of high doses of vitamin D on fertility is unknown.

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

Refined olive oil

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

2 years
Once opened, use within 5 months.

6.4 Special precautions for storage

Store in the original package in order to protect from the light.
Do not freeze.

6.5 Nature and contents of container

20 ml type III amber glass bottle containing 10 ml (corresponding to 400 drops), closed with a child-resistant polypropylene screw cap.
The pack contains 1 bottle and 1 type III glass dropper applicator, with a small nitrile rubber bulb in a separate polypropylene protective case.
OR
20 ml type III amber glass bottle containing 10 ml (corresponding to 400 drops) including an inserted polyethylene dropper, closed with a child-resistant polyethylene screw cap.

6.6 Special precautions for disposal and other handling

Instructions for Use

For packs with an external (separate) dropper:
1. Press on the cap of the bottle and unscrew simultaneously;
2. Remove the cap;
3. Take the dropper and unscrew the protective case;
4. Place the dropper into the bottle to remove the contents;
5. Transfer the required number of drops onto a spoon;
6. Return the empty dropper to its protective case;
7. Screw the cap to close the bottle;
8. Return bottle and dropper to the carton.

For packs with an inserted dropper:
1. Press on the cap of the bottle and unscrew simultaneously;
2. Remove the cap;
3. The bottle should be held vertically while dispensing drops onto a spoon.
4. Screw the cap to close the bottle.
5. Return the bottle to the carton.

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

Do not store any product or food mixture that contains Fultium for use at a later time or a next meal.

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