SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cholecalciferol Viatris 10.000 IE, zachte capsules
Cholecalciferol Viatris 25.000 IE, zachte capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cholecalciferol Viatris 10.000 IE, zachte capsules
Each soft capsule contains: Cholecalciferol (vitamin D_3) 0.250 mg corresponding to 10,000 IU.

Cholecalciferol Viatris 25.000 IE, zachte capsules
Each soft capsule contains: Cholecalciferol (vitamin D_3) 0.625 mg corresponding to 25,000 IU.

Excipients with known effect: glycerol.

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Cholecalciferol Viatris 10.000 IE, zachte capsules are bourgogne red, size 2, oblong, soft capsules containing a clear colourless or greenish-yellow transparent solution

Cholecalciferol Viatris 25.000 IE, zachte capsules are bourgogne red, size 4, oblong, soft capsules containing a clear colourless or greenish-yellow transparent solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Prevention and treatment of vitamin D deficiency in adults.
Prevention of vitamin D deficiency for 25,000 UI only in adults with an identified risk when therapeutic adherence (or compliance) is not achieved by daily administration of low cholecalciferol doses.

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. The patient's dietary habits should be carefully evaluated and artificially added vitamin D content of certain food types should be taken into consideration. Cholecalciferol Viatris 10.000 IE, zachte capsules are suitable for weekly vitamin D supplementation. Cholecalciferol Viatris 25.000 IE, zachte capsules are suitable for weekly (treatment) and monthly (prevention) vitamin D supplementation.
Dosage should be established by a physician.

Cholecalciferol Viatris 10.000 IE, zachte capsules
Adults
Prevention of vitamin D deficiency: 1 capsule every 2 weeks. In a population at high risk of vitamin D deficiency (see below), the dosage could be increased to 1 capsule weekly.

Treatment of vitamin D deficiency: 2 capsules weekly for up to 4-12 weeks.
After first month, a lower maintenance dose should 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. The duration of use is usually limited to the first month of treatment, depending on the doctor's decision. Medical supervision is necessary as dose requirements may vary dependent on patient response (see section 4.4).
Higher doses could be necessary in some patients with vitamin D deficiency, where the dose should be adjusted dependent upon desirable serum levels of 25-hydroxycholecalciferol (25(OH)D), the severity of the disease and the patient´s response to treatment.

Cholecalciferol Viatris 25.000 IE, zachte capsules
Adults
Prevention of vitamin D deficiency in adults with an identified risk when therapeutic adherence (or compliance) is not achieved by daily administration of low cholecalciferol doses: 1 capsule monthly. In a population at high risk of vitamin D deficiency (see below), the dosage could be increased to 2 capsules monthly.

Treatment of vitamin D deficiency: 1 capsule weekly for up to 4-12 weeks.
After first month, a lower maintenance dose should 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. The duration of use is usually limited to the first month of treatment, depending on the doctor's decision. Medical supervision is necessary as dose requirements may vary dependent on patient response (see section 4.4).
Higher doses could be necessary in some patients with vitamin D deficiency, where the dose should be adjusted dependent upon desirable serum levels of 25-hydroxycholecalciferol (25(OH)D), the severity of the disease and the patient's response to treatment.

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 with osteoporosis.
- Use of certain concomitant medications (e.g., anticonvulsant medications, glucocorticoids).
- Patients with malabsorption, including inflammatory bowel disease and coeliac disease.

Special populations

Renal impairment
Cholecalciferol soft capsules should not be used in patients with severe renal impairment (see section 4.3).

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

Paediatric population
Cholecalciferol soft capsules should not be used in children under 18 years.

Pregnancy and breastfeeding
Cholecalciferol soft capsules should not be used in pregnancy and breastfeeding.

4.3 Contraindications

- Hypersensitivity to cholecalciferol or to any of the excipients listed in section 6.1.
- Diseases/conditions associated hypercalcaemia and/or hypercalciuria.
- Calcium nephrolithiasis, nephrocalcinosis
- Hypervitaminosis D.
- Severe renal impairment (see section 4.4).

4.4 Special warnings and precautions for use

In case of long-term administration at high doses, it is advised to monitor serum levels of 25–hydroxyl cholecalciferol. Intake of Cholecalciferol Viatris, zachte capsules should be stopped when serum levels of 25–hydroxyl cholecalciferol exceed 100 ng/ml (corresponding to 250 nmol/l).

In patients already receiving cardiac glycosides or diuretics it is important to monitor calcaemia and calciuria. In case of hypercalciuria or renal insufficiency, the dose should be reduced or the treatment discontinued.

To avoid overdose, the total dose of vitamin D must be taken into consideration in case of combination with treatments containing vitamin D, food added with vitamin D, or in case milk enriched with vitamin D is used.

A dosage increase compared to those indicated may be required in the following cases:

- Subjects treated with anticonvulsants and barbiturates (see section 4.5);
- Subjects treated with corticosteroid therapies (see section 4.5);
- Subjects treated with lipid-lowering agents such as colestipol, colestyramine and orlistat (see section 4.5)
- Subjects treated with antiacids containing aluminium (see section 4.5);
- Obese subjects (see section 5.2);
- Digestive disorders (intestinal malabsorption, mucoviscidosis, or cystic fibrosis);
- Hepatic insufficiency.

The product should be prescribed with caution in patients suffering from sarcoidosis, due to the possible increased metabolism of active vitamin D. Plasma and urinary calcium levels should be monitored in these patients.

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 is not metabolised normally and other forms of vitamin D should be used (see section 4.3).

During long-term treatment with high doses of vitamin D calciuria and renal function, especially in elderly patients, must be monitored. It is recommended to reduce the dose or interrupt treatment if the calcium content in the urine exceeds 7.5 mmol / 24 hours (300 mg / 24 hours).

The product should not be taken by patients with a predisposition to calcium-containing kidney stones.

Any need to add calcium supplements should be considered individually on a case-by case basis. Calcium supplements should be given under strict medical control.

Cholecalciferol 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.

Paediatric population
Cholecalciferol soft capsules should not be given to infants and children under 18 years.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use of anticonvulsants or barbiturates can reduce the effect of vitamin D3 due to metabolic inactivation (phenytoin, phenobarbital, primidone, etc.).

In case of therapy with thiazide diuretics reducing calcium urinary excretion, serum calcium levels should be monitored.

Concomitant use of glucocorticoids can reduce the effect of vitamin D_3.

In case of treatment with drugs containing digitalis and other cardiac glycosides, oral administration of calcium combined with vitamin D may increase the risk of digitalis toxicity (arrhythmia). Medical control is therefore required as well as ECG and serum calcium levels monitoring, if required.

Concomitant use of antiacids containing aluminium can interfere with the drug efficacy, reducing vitamin D absorption, while preparations containing magnesium may expose to a risk of hypermagnesemia.

Studies on animals have suggested a possible potentiation of warfarin action when given with calciferol. Although there is no such evidence with the use of cholecalciferol, caution is appropriate when the two drugs are used concomitantly.

Colestyramine, colestipol, orlistat and laxatives (such as paraffin oil) may reduce vitamin D absorption, while chronic alcoholism reduces vitamin D deposits in the liver.

Rifampicin may reduce cholecalciferol efficacy due to hepatic enzyme induction.

Isoniazide may reduce cholecalciferol efficacy due to the inhibition of metabolic activation 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.

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

Pregnancy
Cholecalciferol soft capsules 10.000 and 25.000 UI is not indicated during pregnancy due to the lack of clinical data.. High doses of vitamin D have been shown to have teratogenic effects in animal experiments (see section 5.3). Overdose in the first 6 months of pregnancy may have toxic

effects on the foetus: there is a correlation between excessive intake of or extremely maternal sensitiveness to vitamin D during pregnancy and physical and mental retardation, supravalvular aortic stenosis and retinopathy of the child.
Maternal hypercalcaemia can also lead to the suppression of parathyroid function in infants with consequent hypocalcaemia, tetany and convulsions.
However, during pregnancy and breast-feeding adequate vitamin D intake is necessary and lower dosed products should be used, when needed.
Where there is a vitamin D deficiency the recommended dose is dependent on national guidelines.

Lactation
Vitamin D3 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

Cholecalciferol soft capsules has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

In general cholecalciferol is well tolerated. Adverse reactions are listed by system organ class and frequency. Frequencies are defined as:
Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000) and not known (cannot be estimated from the available data).

Immune system disorders:
Uncommon: Hypersensitivity reactions

Metabolism and nutrition disorders:
Uncommon: Hypercalciuria, hypercalcaemia, weakness, anorexia, thirst in case of prolonged administration.

Psychiatric disorders:
Rare: Drowsiness, confusion.

Nervous system disorders:
Not known: Headache.

Gastrointestinal disorders:
Rare: Constipation, flatulence, abdominal pain, nausea, vomiting, diarrhoea, metal taste, dry mouth.

Skin and subcutaneous tissue disorders:
Rare: Rash, pruritus, urticarial

Renal and urinary disorders:
Not known: Nephrocalcinosis, polyuria, polydipsia, renal failure.

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

Vitamin D intoxication is a consequence of accidental or intentional poisoning as well as of chronic overdose. Acute or chronic overdose occurs as hypercalciuria and hypercalcaemia, whose symptoms include headache, anorexia, diarrhoea, constipation, nausea, vomiting, thirst, polyuria, kidney stones, dehydration, lethargy and subsequent renal failure with also fatal outcome in rare cases.
Chronic overdoses can also lead to vascular and organ calcification as a result of hypercalcemia.

In rare cases hypercalcaemia was lethal.

Treatment in case of overdose
Stop Cholecalciferol soft capsules and proceed to rehydration.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues, cholecalciferol
ATC Code: A11CC05
Cholecalciferol is produced within the skin under the influence of UV radiation including sunlight. In its biologically active form, cholecalciferol 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 cholecalciferol. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active cholecalciferol.

5.2 Pharmacokinetic properties

As for other liposoluble vitamins, cholecalciferol intestinal absorption is promoted by concomitant intake of fat foods.

Absorption
Cholecalciferol is easily absorbed in the small intestine.

Cholecalciferol is present in the blood circulation in combination with specific a-globulins that transport it to the liver, where it is hydroxylated to 25-hydroxy cholecalciferol. A second hydroxylation occurs in the kidneys, where 25-hydroxy cholecalciferol is transformed into 25-dihydroxy cholecalciferol, representing the active metabolite of vitamin D that is responsible for the effects on phosphate and calcium metabolism.

Unchanged cholecalciferol is stored in the muscle and fatty tissue in order to be available based on the body needs. In obese subjects, vitamin D bioavailability is reduced due to the exceeding fatty tissue.

Vitamin D is eliminated via the faeces and urine.

5.3 Preclinical safety data

Preclinical studies carried out on different animal species show that toxic effects occurs in animals only at doses clearly exceeding therapeutic doses in humans.

The effects most commonly detected in repeated dose toxicity studies are: increased calciuria, decreased phosphaturia and proteinuria.

Hypercalcaemia was observed at high doses. In case of prolonged hypercalcaemia, the most frequent histological alterations (calcifications) affected kidneys, heart, aorta, testicles, thymus and intestinal mucosa.

Cholecalciferol has no teratogenic activity at doses that are equivalent to therapeutic doses. At doses far higher than the human therapeutic range, the teratogenicity has been observed in animal studies.

Cholecalciferol has no mutagenic and carcinogenic potential.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Cholecalciferol 10,000 IU, 25,000 IU soft capsules:
Fill:
olive oil refined,
Butylhydroxytoluene (E321).

Shell:
glycerol (E422),
titanium dioxide (E171),
gelatine
allura Red 40 (E129).

6.2 Incompatibilities

Any incompatibility with other drugs is not known.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Store below 25°C in the original package to protect from light.

Do not freeze.

6.5 Nature and contents of container

Cholecalciferol Viatris 10.000 IE, zachte capsules
Opaque white PVC/PVDC and Aluminium thermo-sealed blister packed in cardboard box. The pack contains 2, 4, 8, 10 capsules.

Cholecalciferol Viatris 25.000 IE, zachte capsules
Opaque white PVC/PVDC and Aluminium thermo-sealed blister packed in cardboard box. The pack contains 1, 2, 4, capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

RVG 132323 Cholecalciferol Viatris 10.000 IE, zachte capsules

RVG 132324 Cholecalciferol Viatris 25.000 IE, zachte capsules

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 4 januari 2024

10. DATE OF REVISION OF THE TEXT