SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cholecalciferol Teva 20.000 IE, zachte capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 0.500 mg cholecalciferol, equivalent to 20 000 IU vitamin D_3.

Excipient with known effect
The capsules may contain trace amounts of soya lecithin (may contain soya oil).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

soft capsules.

Orange, opaque, oval-shaped, soft capsule filled with clear, slightly yellow, oily liquid.
Dimension: Length: approx. 8-9 mm, Width: approx. 6-7 mm

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Initial treatment of clinically relevant vitamin D deficiency (serum levels <25 nmol/l or <10 ng/ml) 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 patient's dietary habits should be carefully evaluated and artificially added vitamin D and calcium content of certain food types should be taken into consideration.

Adults
Recommended dose: One capsule (20 000 IU) per week for up to 4-5 weeks.

After the first month, a lower maintenance dose should be considered according to the desirable serum levels of 25-hydroxycholecalciferol (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
<Product name> must not be used in patients with severe renal impairment (see section 4.3).

Paediatric population
<Product name> should not be used in children and adolescents. The strength of 20 000 IU soft capsules is not suitable for the use in paediatric population because studies on the safe use of high doses in paediatric population are too limited. However, products with a strength lower than 20 000 are also available.

Method of administration

The capsules 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.
- Nephrocalcinosis
- Diseases and/or conditions resulting in hypercalcaemia or hypercalciuria.
- Severe renal impairment (see section 4.4)
- Peanut or soya allergy

4.4 Special warnings and precautions for use

Monitoring
During the initial treatment, serum calcium levels should be followed and renal function should be monitored through measurements of serum creatinine. Monitoring is especially important in elderly patients on concomitant treatment with cardiac glycosides or diuretics (see section 4.5), patients with a tendency to form kidney stones and immobilised patients. In case of hypercalciuria (exceeding 300 mg (7.5 mmol)/24 hours) treatment has to be discontinued. In case of signs of impaired renal function the dose should be reduced or the treatment discontinued.

Sarcoidosis
Cholecalciferol should be prescribed with caution to patients suffering from sarcoidosis due to risk of increased metabolism of vitamin D into its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Renal impairment
Cholecalciferol 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. <Product name> must not be used in patients with severe renal impairment (see section 4.3), since vitamin D_3 may not be metabolised normally.

Concomitant use of multivitamin products
The content of vitamin D in this medicinal product should be considered when prescribing other vitamin D metabolites and analogues, as well as food supplements containing vitamin D. Additional doses of vitamin D should be taken under close medical supervision.

Pseudohypoparathyroidism
Vitamin D is not recommended 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.

Lecithin from soya
This medicine contains traces of lecithin from soya, which may contain soya oil. Not to be used in case of allergy to peanut or soya.

4.5 Interaction with other medicinal products and other forms of interaction

Thiazide diuretics
Thiazide diuretics reduce the urinary excretion of calcium. Due to the increased risk of hypercalcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics.

Phenytoin or barbiturates
Concomitant use of phenytoin or barbiturates may reduce the effect of vitamin D since the metabolism increases.

Glucocorticoids
Glucocorticoid steroids may increase vitamin D metabolism and elimination. During concomitant use, it may be necessary to increase the dose of cholecalciferol.

Digitalis
Excessive dosing of vitamin D can induce hypercalcaemia, which may increase the risk of digitalis toxicity and serious arrhythmias due to the additive inotropic effects. The electrocardiogram (ECG) and serum calcium levels of patients should be closely monitored.

Resins, laxatives and orlistat
Simultaneous treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D. Orlistat may potentially impair the absorption of cholecalciferol, as it is fat-soluble.

Actinomycin and imidazoles
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.

Magnesium
Products containing magnesium (such as antacids) should not be taken during treatment with high doses of vitamin D_3 because of the risk of hypermagnesemia.

Phosphor
Products containing phosphor used in large doses, given concomitantly may increase the risk of hyperphosphatemia.

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

Isoniazid
Isoniazid may reduce the effectiveness of cholecalciferol due to inhibition of the metabolic activation of cholecalciferol

4.6 Fertility, pregnancy and lactation

Pregnancy
The recommended daily intake for pregnant women is 600 IU, however, in women who are considered to be vitamin D deficient a higher dose may be required. 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.

There are no or limited amount of data from the use of cholecalciferol in pregnant women. Studies in animals have shown reproductive toxicity at high doses. 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 (See section 5.3).

Where there is a vitamin D deficiency the recommended dose is dependent on national guidelines, however, the maximum recommended dose during pregnancy is 4,000 IU/day vitamin D_3 (0.100 mg cholecalciferol). <Product name> is not recommended during pregnancy.

Breastfeeding
Vitamin D_3 and metabolites are excreated into the breast-milk. High-dose vitamin D should not be used during breast-feeding. Overdose in infants induced by nursing mothers has not been observed; however, when prescribing additional vitamin D to a breast-fed child the practitioner should consider the dose of any additional vitamin D given to the mother.

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 effects of cholecalciferol 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), rare (≥1/10,000, <1/1,000) or 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 angioedema 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 listed in Appendix V.

4.9 Overdose

The most serious conseqence of acute or chronic overdose is hypercalcaemia due to vitamin D toxicity. Symptoms of hypercalcaemia may include anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, mental disturbances, polydipsia, polyuria, bone pain, nephrocalcinosis, renal calculi and in severe cases, cardiac arrhythmias. Extreme hypercalcaemia may result in coma and death.

Persistently high calcium levels may lead to irreversible renal damage and soft tissue calcification.

Treatment of hypercalcaemia: The treatment with vitamin D must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A, and cardiac glycosides must also be discontinued. Rehydration, and, according to severity, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids should be considered. Serum electrolytes, renal function and diuresis

must be monitored. In severe cases, ECG and CVP should be followed. Depending on the degree of hypercalcaemia and on the patient's condition, e.g. in case of oligoanuria, haemodialysis (calcium-free dialysate) may be necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues, cholecalciferol
ATC Code: A11CC05

In its biologically active form, vitamin D_3 stimulates calcium absorption, the incorporation of calcium into the osteoid and the release of calcium from the bone tissue. In the small intestine, it promotes rapid and delayed absorption of calcium. The passive and active transport of phosphate is also stimulated. In the kidney, it inhibits the excretion of calcium and phosphate by promoting tubular reabsorption. The formation of parathyroid hormone (PTH) in the parathyroid glands is directly inhibited by the biologically active form of vitamin D_3. PTH secretion is also inhibited by increased calcium absorption in the small intestine under the influence of biologically active vitamin D_3.

5.2 Pharmacokinetic properties

Absorption
Vitamin D is easily absorbed in the small intestine.

Distribution and biotransformation
Cholecalciferol and its metabolites circulate in the blood bound to a specific globulin. Cholecalciferol is converted in the liver by hydroxylation to 25- hydroxycholecalciferol. It is then further converted in the kidneys to 1,25- dihydroxycholecalciferol. 1,25-dihydroxycholecalciferol is the active metabolite responsible for increasing calcium absorption. Vitamin D, which is not metabolised, is stored in adipose and muscle tissues.

Elimination
Vitamin D is excreted mainly in bile and faeces with a small percentage found in urine.

5.3 Preclinical safety data

Effects in non-clinical single and repeat-dose toxicity studies have been observed only at exposures of high doses. At doses far higher than the human therapeutic range teratogenicity has been observed in animal studies. Normal endogenous levels of cholecalciferol have no potential mutagenic activity (negative in Ames-test) and no carcinogenic activity. No other relevant data is available that has not been mentioned elsewhere in the SmPC (see section 4.6 and 4.9).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule fill
Triglycerides, medium-chain
all-rac-α-Tocopherol (E307)

Capsule shell
Gelatin
Glycerol (E422)
Titanium dioxide (E171)

Iron oxide yellow (E172)
Iron oxide red (E172)
Purified water
Trace substances of phosphatidylcholine (from soybean), caprylic/capric triglycerides, ethanol, glyceride (from sunflower seed oil), oleic acid, ascorbyl palmitate and α-tocopherol.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25 °C. Store in the original package, in order to protect from light and moisture. Keep blisters in the outer carton.

6.5 Nature and contents of container

PVC/PVDC-Aluminium unit-dose blister packs of 1, 4x1, 5x1, 10x1, 30x1 and 50x1 soft capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

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

7. MARKETING AUTHORISATION HOLDER

Teva B.V.
Swensweg 5
2031 GA Haarlem
Nederland

8. MARKETING AUTHORISATION NUMBER(S)

RVG 130081

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 29 september 2023

10. DATE OF REVISION OF THE TEXT

Laatste gedeeltelijke wijziging betreft rubriek 6.5: 25 december 2024.