SUMMARY OF PRODUCT CHARACTERISTICS

1. NAAM VAN HET GENEESMIDDEL

Vitamine D3 Teva 25.000 IE, zachte capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<PRODUCT NAME> 25,000 IU capsules, soft
Each capsule contains 0.625 mg cholecalciferol (vitamin D3), equivalent to 25,000 IU vitamin D3.

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

Capsule, soft.

Yellow, opaque, oval soft gelatin capsule with dimension of approximately 9 mm x 6 mm.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Initial treatment of clinically relevant vitamin D deficiency in adults (serum level <25 nmol/L (<10 ng/mL)).

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

Hepatic impairment
No dose adjustment is required.

Renal impairment
<PRODUCT NAME> must not be used in patients with severe renal impairment.

Paediatric population
<PRODUCT NAME> is not recommended for use in children and adolescents under 18 years of age.

Method of administration
The capsules should be swallowed whole with water.
Patients should be advised to take <PRODUCT NAME> preferably with a meal.

4.3 Contraindications

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- hypercalcaemia and/or hypercalciuria
- nephrolithiasis
- nephrocalcinosis
- severe renal impairment

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.

4.4 Special warnings and precautions for use

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.

Monitoring calcium
During treatment with cholecalciferol, calcium levels in serum and urine 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 and patients with a tendency to form kidney stones. 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.

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. In patients with severe renal insufficiency, <PRODUCT NAME> is contraindicated.

Other vitamin D intake
The content of vitamin D in <PRODUCT NAME> 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. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.

Pseudohypoparathyroidism
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.

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

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.

Medicinal products that augment the vitamin D effect

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.

Medicinal products that decrease the vitamin D effect

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.

Resins and laxatives
Simultaneous treatment with ion exchange resins such as cholestyramine, orlistat or laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D.

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.

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

During pregnancy and breast-feeding this high dosed product is not recommended and a lower dosed product should be used.
During pregnancy and breast-feeding adequate vitamin D intake is necessary. The recommended daily intake level for vitamin D during pregnancy and lactation following national guidelines is only around 600 IU.

Pregnancy
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. High doses of vitamin D have been shown to have teratogenic effects in animal experiments (see section 5.3).

However, overdose of vitamin D must be avoided during pregnancy, as prolonged hypercalcaemia may 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 recommended dose during pregnancy is 4,000 IU/day vitamin D3. For treatment during pregnancy at higher doses, <PRODUCT NAME> is not recommended during pregnancy.

Breast-feeding
High-dose vitamin D should not be used during breastfeeding. Vitamin D and its metabolites pass into breast milk. If treatment with vitamin D is clinically indicated during breastfeeding this should be considered when giving additional vitamin D to the child.

Fertility
There are no data on the effect of cholecalciferol 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 cholecalciferol on the ability to drive. However, an effect on this ability is unlikely.

4.8 Undesirable effects

Adverse reactions frequencies as defined as: uncommon (≥1/1,000 to <1/100), rare (≥ 1/10,000 to <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

Overdose can lead to hyper-vitaminosis D. An excess of vitamin D causes abnormally high levels of calcium in the blood, which can eventually severely damage the soft tissues, and kidneys.

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 central venous pressure 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 D3 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 D3. PTH secretion is also inhibited by increased calcium absorption in the small intestine under the influence of biologically active vitamin D3.
Other functions of the biologically active vitamin D3 include cell differentiation and antiproliferative actions in various cell types, such as bone marrow (osteoclast precursors and lymphocytes), cells belonging to the immune system, skin, breast and prostate epithelial cells, muscle and intestine.

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.
Cholecalciferol and its metabolites are excreted mainly in the bile and faeces.

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 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 further no information of relevance to the safety assessment in addition to what is stated in other parts of 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 E441
Glycerol E422
Titanium dioxide E171
Iron oxide yellow E172
Purified water
Trace substances of triglycerides, medium-chain, lecithin/phosphatidylcholine (from soybean), caprylic/capric triglycerides, ethanol, glyceride (from sunflower seed oil), oleic acid, ascorbyl palmitate and 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 moisture.

6.5 Nature and contents of container

PVC/PVDC/aluminium blister (250 µm / 90 gsm / 20 µm), packs of 1, 2, 3, 4, 6, 12 and 50 soft capsules; unit dose blister packs of 3x1, 4x1, 6x1, 12x1 and 50x1 soft capsules; and hospital packs of 12 and 50 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. HOUDER VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

Teva B.V.
Swensweg 5
2031 GA Haarlem
Nederland

8. NUMMER(S) VAN DE VERGUNNING VOOR HET IN DE HANDEL BRENGEN

RVG 128280

9. DATUM VAN EERSTE VERLENING VAN DE VERGUNNING/VERLENGING VAN DE VERGUNNING

Datum van eerste verlening van de vergunning: 24 mei 2022

10. DATUM VAN HERZIENING VAN DE TEKST

Laatste gedeeltelijke wijziging betreft rubriek 6.5: 1 februari 2024