

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cholecalciferol Heumann 20.000 IE, zachte capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains 500 micrograms cholecalciferol (vitamin D₃, equivalent to 20 000 IU)

Excipient(s) with known effect:

Each soft capsule contains 14.4 mg sorbitol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule, soft (Capsule)

Reddish orange transparent oval shaped soft gelatin capsule containing clear colorless liquid with dimensions 9.5 ± 1 mm long x 5.5 ± 1 mm wide.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Initial treatment of clinically relevant vitamin D deficiency (serum level 25 (OH)D < 25 nmol/l) 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.

Special populations:

Renal impairment

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

Hepatic impairment

No dose adjustment is necessary in patients with hepatic impairment.

Pediatric population

Cholecalciferol Heumann should not be used in children < 18 years of age. Other cholecalciferol products are available.

Method of administration

Oral

Cholecalciferol Heumann are taken orally and 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 or conditions resulting in hypercalcaemia and/or hypercalciuria
- Severe renal impairment

4.4 Special warnings and precautions for use

Monitoring

During initial and long-term treatment with cholecalciferol, serum and urinary calcium levels should be monitored and renal function checked by measuring serum creatinine level. These controls are especially important in elderly patients and in concomitant treatment with cardiac glycosides or diuretics. In case of hypercalcaemia or signs of reduced renal function, the dose should be reduced or treatment interrupted. It is recommended to reduce the dose or interrupt treatment if the urinary calcium level exceeds 7.5 mmol/24 hours (300 mg/24 hours).

Renal impairment

Vitamin D₃ should be used with caution in patients with renal impairment, as these patients have a higher risk of hypercalcaemia. The effects on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account. Vitamin D₃ must not be used in patients with severe renal insufficiency (see section 4.3), as vitamin D₃ is not metabolized normally.

Sarcoidosis

Cholecalciferol should be prescribed with caution in patients suffering from sarcoidosis because of the risk of increased metabolism of vitamin D₃ to its active form. Serum and urine calcium levels should be monitored in these patients.

Pseudohypoparathyroidism

The use of cholecalciferol 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.

Other vitamin D₃-containing products

The vitamin D content in Cholecalciferol Heumann should be considered when prescribing other medications containing vitamin D₃. Supplemental administration of vitamin D₃ should be done only under medical supervision.

Paediatric population

Cholecalciferol Heumann is not indicated for use in children and adolescents.

Sorbitol

This medicinal product contains sorbitol. The additive effect of concomitantly administered products

containing sorbitol (or fructose) and dietary intake of sorbitol (or fructose) should be taken into account.

The content of sorbitol in medicinal products for oral use may affect the bioavailability of other medicinal products for oral use administered concomitantly.

4.5 Interaction with other medicinal products and other forms of interaction

Calcium-containing products

Concomitant use with calcium-containing products administered in large doses may increase the risk of hypercalcemia.

Diuretics

Thiazide diuretics reduce the urinary excretion of calcium. Regular monitoring of serum calcium levels is necessary in the case of concomitant use of thiazide diuretics or with calcium-containing products taken in large doses because of an increased risk of hypercalcemia.

Phenytoin and barbiturates

Concomitant treatment with phenytoin or barbiturates may reduce the effect of vitamin D₃ due to metabolic activation.

Digitalis and other cardiac glycosides

The effects of digitalis and other cardiac glycosides may be accentuated with the oral administration of calcium combined with vitamin D₃. Strict medical supervision is required and, if necessary, monitoring of ECG and calcium.

Ion-exchange resins, laxatives and drugs that lead to malabsorption of fat

Concomitant treatment with ion-exchange resins (e.g., cholestyramine) or laxatives (such as paraffin oil) may reduce the gastrointestinal absorption of vitamin D₃. Products that lead to malabsorption of fat, e.g., orlistat, may interfere with vitamin D₃ absorption.

Actinomycin and imidazole antimycotics

The cytotoxic agent actinomycin and imidazole antifungal agents interfere with vitamin D₃ activity by inhibiting the conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D by the renal enzyme 25-hydroxyvitamin D-1-hydroxylase.

Systematic corticosteroids

Systematic corticosteroids inhibit the absorption of calcium. Long-term use of corticosteroids may offset the effect of vitamin D₃.

Magnesium-containing products

Products containing magnesium (like antacids) should not be taken during long-term treatment with high doses of vitamin D₃ because of the risk of hypermagnesemia.

Phosphor-containing products

Products containing phosphor used in large doses and given concurrently may increase the risk of hyperphosphataemia.

Rifampicin and isoniazid

Rifampicin may also reduce the efficacy of vitamin D₃ by induction of liver enzymes.

Isoniazid may reduce the efficacy of vitamin D₃ by inhibition of metabolic activation of vitamin D₃.

4.6 Fertility, pregnancy and lactation

During pregnancy and breastfeeding this high dosed product is not recommended, and a lower dosed product should be used.

During pregnancy and breastfeeding 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

Overdose of vitamin D should be avoided during pregnancy, as prolonged hypercalcaemia can lead to physical and mental retardation, supraaortic stenosis, and retinopathy of the child.

During pregnancy the daily intake should not exceed 4 000 IU vitamin D. Studies in animals have shown reproductive toxicity of high doses of vitamin D (see section 5.3).

Breastfeeding

High-dose vitamin D should not be used during breastfeeding. Vitamin D and its metabolites pass into breast milk. If treatment with Cholecalciferol Heumann is clinically indicated during breastfeeding, 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

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

4.8 Undesirable effects

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1\ 000$ to $< 1/100$), rare ($\geq 1/10\ 000$ to $< 1/1\ 000$), very rare ($< 1/10\ 000$), not known (cannot be estimated from the available data).

The side effects result from overdose.

Immune system disorders:

not known (cannot be estimated from the available data): Hypersensitivity reactions such as angio-oedema or laryngeal oedema.

Metabolism and nutrition disorders:

Uncommon: hypercalcaemia and hypercalciuria.

Gastrointestinal disorders:

Not known: constipation, flatulence, nausea, abdominal pain, diarrhea.

Skin and subcutaneous disorders:

Rare: Pruritus, rash and urticaria.

Hypercalcemia

Depending on the dose and duration of the treatment, severe and persistent hypercalcemia with acute (cardiac arrhythmias, nausea, vomiting, mental symptoms, disturbances of consciousness) and chronic (increased urination, increased thirst, loss of appetite, weight loss, kidney stones, renal calcification, calcification of tissues outside the bone) consequences may occur. Fatal outcome has been reported in very rare cases (see also sections 4.4, 4.5 and 4.9).

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

Symptoms of overdose

Overdose leads to elevated serum and urinary phosphor levels, as well as hypercalcemia and consequent calcium deposits in the tissues and especially in the kidneys (nephrolithiasis, nephrocalcinosis) and vessels.

The symptoms of intoxication are uncharacteristic and manifest as nausea, vomiting, diarrhea often in the early stages and later obstipation, loss of appetite, headache, muscle and joint pain, muscle weakness, fatigue, mental disturbance, nephrocalcinosis, renal calculi, pancreatitis, polydipsia, polyuria and in the final stage dehydration. In severe cases, cardiac arrhythmias can occur. Typical biochemical findings include hypercalcemia, hypercalciuria and elevated serum concentrations of 25-hydroxycolecalciferol.

Treatment of overdose

Symptoms of chronic overdose with vitamin D₃ may require both forced diuresis and administration of glucocorticoids or calcitonin.

Overdosage requires measures to treat hypercalcemia - often persistent and, under certain circumstances, life-threatening. The first measure is to discontinue the vitamin D₃ preparation (and calcium supplements); it takes several weeks to normalize hypercalcemia caused by vitamin D₃ intoxication. Depending on the degree of hypercalcemia, measures include a low or calcium-free diet, administration of oral or intravenous fluids, increase in urinary excretion through the drug furosemide, as well as administration of glucocorticoids and calcitonin. In severe cases, haemodialysis with calcium-free dialysate may be required.

A specific antidote does not exist.

It is recommended that patients chronically treated with higher doses of vitamin D₃ should be made aware of the symptoms of possible overdose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vitamin D and analogues, cholecalciferol, ATC-code: A11CC05

Cholecalciferol (vitamin D₃) is formed in the skin on exposure to UVB light and converted to its biologically active form, 1,25-dihydroxycholecalciferol, in two hydroxylation steps, first in the liver (position 25) and then in renal tissue (position 1). Along with parathormone and calcitonin, 1,25-dihydroxycholecalciferol has a considerable impact on the regulation of calcium and phosphate metabolism. In vitamin D₃ deficiency, the skeleton does not calcify (resulting in rickets) or decalcification of bones occurs (resulting in osteomalacia).

According to production, physiological regulation and mechanism of action, vitamin D₃ is to be considered a precursor of a steroid hormone. In addition to physiological production in the skin, cholecalciferol can be supplied via the diet or in a form of a drug. Since in the latter case the product inhibition of cutaneous vitamin D₃ synthesis is circumvented, overdose and intoxications may occur.

Fish liver oil and fish are particularly rich in vitamin D₃. Small amounts are found in meat, egg yolks, milk, dairy products and avocado.

5.2 Pharmacokinetic properties

Absorption

Cholecalciferol is absorbed up to 80% in the small intestine by passive diffusion after incorporation into mixed micelles. Vitamin D₃ absorption not only occurs by passive diffusion but includes, at least in part, cholesterol transporters. Fat-soluble vitamin D₃ is absorbed through the small intestine in the presence of bile acids by micelle formation and gets into the blood through the lymphatic circulation. Thus, intake during the main meal of the day could facilitate vitamin D₃ absorption.

Distribution

Following absorption, vitamin D₃ enters the blood as part of chylomicrons and then associates primarily with a specific α -globulin. Vitamin D₃ is rapidly distributed, mostly to the liver where it is metabolized to 25-hydroxyvitamin D₃, the major storage form. Lesser amounts are distributed to fat and tissue and stored at these sites as vitamin D₃ for later release to the blood circulation.

Biotransformation

Cholecalciferol is rapidly metabolized by hydroxylation in the liver to 25-hydroxyvitamin D₃ and subsequently metabolized in the kidney to 1,25-dihydroxyvitamin D₃, the biologically active form. Further hydroxylation occurs prior to elimination. A small percentage of vitamin D₃ undergoes glucuronidation before elimination.

After a single oral dose of cholecalciferol, maximum serum concentrations of the primary preservative form are reached after approximately 7 days. 25(OH)D₃ is then slowly eliminated with an apparent half-life in serum of about 50 days. Cholecalciferol and its metabolites are excreted primarily in bile and feces.

Elimination

Vitamin D₃ and its metabolites are excreted primarily in the bile and feces and only slightly via the urine. They undergo extensive enterohepatic recirculation.

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 have no potential mutagenic activity (negative in Ames-test and combined micronucleus with Comet-Assay) and no clinically relevant carcinogenic activity.

There is further no information of relevance to the safety assessment in addition to what is stated in other parts of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule-content

Triglycerides, medium-chain
Butylated hydroxyanisole (E 320)
Butylated hydroxytoluene (E 321)

Capsule shell

Gelatin (E 441)
Glycerol (E 422)

Sorbitol liquid, partially dehydrated (E 420)
Erythrosin (E 127)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for disposal and other handling

Store under 25°C and keep the blister in the original packaging to protect from light.

6.5 Nature and content of container

Blister packs of 1, 6 or 50 soft capsules.

The soft capsules are available in white-opaque PVC/PVdC/Aluminum blister packs.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

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

7. MARKETING AUTHORISATION HOLDER

Heumann Pharma GmbH & Co. Generica KG
Südwestpark 50
90449 Nürnberg
Duitsland

8. MARKETING AUTHORISATION NUMBER

RVG 132575 Cholecalciferol Heumann 20.000 IE, zachte capsules

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 12 december 2023

10. DATE OF REVISION OF THE TEXT

Laatste gedeeltelijke wijziging betreft de rubrieken 2, 4.1, 4.2, 4.4, 4.6, 4.9, 5.1 en 5.3: 27 mei 2025