

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Cholecalciferol Alfrapharma 50.000 IE zachte capsules
Cholecalciferol Alfrapharma 100.000 IE zachte capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Cholecalciferol soft capsules 50 000 IU

Each soft capsule contains: Cholecalciferol (vitamin D₃) 1.250 mg corresponding to 50 000 IU.

Cholecalciferol soft capsules 100 000 IU

Each soft capsule contains: Cholecalciferol (vitamin D₃) 2.500 mg corresponding to 100 000 IU.

Excipients with known effect: allura red n. 40 (E129).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule, soft.

Cholecalciferol 50 000 IU capsule soft are bourgogne red, diameter 9.10 mm and length 13.65 mm, oval, capsule soft containing a clear colourless or greenish-yellow transparent solution.

Cholecalciferol 100 000 IU capsule soft are bourgogne red, diameter 8.60 mm and length 24.07 mm, oval, capsule soft containing a clear colourless or greenish-yellow transparent solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Initial treatment of vitamin D deficiency (serum 25(OH)D < 25 nmol/l) in adults.

4.2 Posology and method of administration

Posology

Adults

The dose should be established by a physician on an individual basis depending on the extent of the necessary vitamin D supplementation. The dose should be adjusted based on the desired serum levels of 25-hydroxyvitamin D (25(OH)D), the severity of the disease, and the patient's response to treatment. 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 soft capsules 50 000 IU capsules

Adults

Treatment of vitamin D deficiency: 1 capsule every 2 weeks

After the first month (for a total of 100 000 IU), a lower dose should be considered based on the desired serum levels of 25-hydroxyvitamin D (25(OH)D), the severity of the disease, and the patient's response to the treatment.

Cholecalciferol soft capsules 100 000 IU capsules

Adults

Treatment of vitamin D deficiency: 1 capsule at once

After the first month (for a total of 100 000 IU.), a lower dose should be considered based on the desired serum levels of 25-hydroxyvitamin D (25(OH)D), the severity of the disease, and the patient's response to the treatment.

Alternatively, it is possible to adhere to national recommendations regarding the dosage for the treatment of vitamin D deficiency,

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 and adolescent under 18 years.

Other suitable products are available.

Method of administration

This medicinal product is for oral use.

The capsule should be swallowed whole with water, preferably with the main meal of the day.

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

Monitoring

During initial and long-term treatment with <Cholecalciferol soft capsules>, serum calcium levels should be monitored and the kidney function checked by measurement of serum creatinine.

These checks are particularly important in elderly patients and in cases of concomitant treatment with cardiac glycosides or diuretics (see section 4.5), as well as in cases of hyperphosphatemia and for patients at higher risk of lithiasis. In the event of hypercalcemia or signs of renal function impairment, it is necessary to reduce the dose or discontinue treatment. It is recommended to reduce the dose or discontinue treatment in case of urinary calcium levels exceeding 7.5 mmol/24 hours (300 mg/24 hours).

Renal impairment

Vitamin D should be used with caution in patients with renal impairment and the effect on the calcium and phosphate metabolism should be monitored. The risk of soft tissue calcification should be taken into account. In patients with severe renal impairment, vitamin D in the form of cholecalciferol is contraindicated as it is not metabolised normally (see section 4.2 and 4.3).

Concomitant administration of other vitamin D-containing products

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.

Sarcoidosis

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.

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.

4.5 Interaction with other medicinal products and other forms of interaction

Products containing calcium

The concurrent use with products containing calcium administered in high doses may increase the risk of hypercalcemia.

Anticonvulsants or barbiturates

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

Thiazide diuretics

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

Glucocorticoids

Concomitant use of glucocorticoids can reduce the effect of vitamin D₃.

Digitalis and other cardiac glycosides

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.

Antiacids

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.

Ion exchange resins and laxatives

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

Rifampicin may reduce cholecalciferol efficacy due to hepatic enzyme induction.

Isoniazide

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

Cytotoxic and antifungal agent

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.

4.6 Fertility, pregnancy and lactation

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 (see section 5.3).

Vitamin D deficiency is harmful for mother and child. However, overdose of vitamin D must be avoided during pregnancy, as prolonged hypercalcaemia may lead to physical and mental retardation, supraventricular 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. Cholecalciferol soft capsules 50 000 IU – 100 000 IU is not recommended during pregnancy.

Breast-feeding

Vitamin D and its metabolites pass into breast milk. Cholecalciferol soft capsules 50 000 IU – 100 000 IU should not be used during breastfeeding. 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 reactions 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 ($\geq 1/10$); 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 ($< 1/10,000$) and not known (cannot be estimated from the available data).

System Organ Class	Uncommon	Rare	Not known
Immune system disorders			Hypersensitivity reactions
Metabolism and nutrition	Hypercalciuria, hypercalcaemia		

System Organ Class	Uncommon	Rare	Not known
disorders			
Gastrointestinal disorders			Constipation, flatulence, abdominal pain, diarrhoea
Skin and subcutaneous tissue disorders		Rash, pruritus, urticarial	

Hypercalcemia

Dependent on dose and duration of treatment of serious and persistent hypercalcemia with its acute (heart rhythm disturbances, dry mouth, metal taste, nausea, vomiting, renal failure, headache, psychiatric symptoms, loss of consciousness) and chronic (polyuria, polydipsia, loss of appetite, weight loss, nephrocalcinosis, kidney calcification, calcification may in tissues outside the bone) episodes occur. Very rarely fatality has been described (see section 4.4 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

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 α -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

Fill:

olive oil refined,
Butylhydroxytoluene (E321).

Shell:

glycerol 98% (E422),
titanium dioxide (E171),
gelatine succinate
allura Red 40 (E129).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.
Store in the original package in order to protect from light.
Do not freeze.

6.5 Nature and contents of container

<Cholecalciferol soft capsules> 50 000 IU – 100 000 IU

Opaque white PVC/PVDC and Aluminium thermo-sealed blister packed in cardboard box.
The pack contains 2 and 4 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Alfrapharma Srl
Viale Manzoni, 59
00185 Rome
Italië

8. MARKETING AUTHORISATION NUMBER(S)

RVG 132431 Cholecalciferol Alfrapharma 50.000 IE zachte capsules
RVG 132432 Cholecalciferol Alfrapharma 100.000 IE zachte capsules

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Datum van eerste verlening van de vergunning: 11 september 2026

10. DATE OF REVISION OF THE TEXT