



## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

DEVIT-3 20,000 IU Soft Capsules

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains:

**Active Substance:**

Cholecalciferol 20,000 IU

(Equivalent to 500 mcg Cholecalciferol)

**Excipient(s) with known effect:**

Sorbitol 6.72 mg

Sunset Yellow FCF (E110) 0.04 mg

For a full list of excipients, see section 6.1.

### 3. PHARMACEUTICAL FORM

Soft capsules.

Biconvex, oval, transparent, orange colored soft capsules.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

DEVIT-3 is indicated in the treatment, maintenance treatment, and prophylaxis of Vitamin D deficiency.

#### 4.2 Posology and method of administration

##### Posology/frequency and duration of administration

Each soft capsule contains 20,000 IU (500 mcg) of Vitamin D<sub>3</sub>. It should not be used in children and infants under 12 years of age.

##### *Pediatric posology*

In the prevention and maintenance treatment of Vitamin D deficiency for 11 to 18 years of age

One soft capsule of DEVIT-3 20,000 IU once a month, equivalent to a daily dose of 400-800 IU, should be used as recommended by the doctor.

In the treatment of Vitamin D deficiency for 11 to 18 years of age

One soft capsule of DEVIT-3 20,000 IU once or twice a week, equivalent to a daily dose of 3,000-5,000 IU, should be used as recommended by the doctor.

##### *Adult posology*

In the prevention and maintenance treatment of Vitamin D deficiency

One soft capsule of DEVIT-3 20,000 IU once or twice a month, equivalent to a daily dose of 600-1,500 IU, should be used as recommended by the doctor.

In the treatment of Vitamin D deficiency

One soft capsule of DEVIT-3 20,000 IU every two days, equivalent to a daily dose of 7,000-10,000 IU, should be used as recommended by the doctor. Follow-up 25(OH)D measurements should be



made approximately three to four months after initiation of maintenance therapy to confirm that the target level has been reached.

The doctor will decide how to use the medicine. It should be used in accordance with the doctor's recommendation.

Age Group	Recommended Dose for Prophylaxis / Maintenance	Vitamin D Deficiency Treatment Dosage		Maximum Tolerated Dose for Long-Term Treatment and Prophylaxis in Risk Groups
		Daily Treatment**	Weekly Administration	
Newborn	400 IU/day (10 mcg/day)	1,000 IU/day (25 mcg/day)	No	1,000 IU/day (25 mcg/day)
1 month to 1 year	400 IU/day (10 mcg/day)	2,000-3,000 IU/day (50-75 mcg/day)	No	1,500 IU/day (37.5 mcg/day)
1 year to 10 years	400-800* IU/day (10-20 mcg/day)	3,000-5,000 IU/day (75-125 mcg/day)	No	2,000 IU/day (50 mcg/day)
11 years to 18 years	400-800* IU/day (10-20 mcg/day)	3,000-5,000 IU/day (75-125 mcg/day)	No	4,000 IU/day (100 mcg/day)
Adults over 18 years	600-1,500 IU/day (15-37.5 mcg/day)	7,000-10,000 IU/day (175-250 mcg/day)	50,000 IU/week (1250 mcg/week)***	4,000 IU/day (100 mcg/day)

\* Can be increased up to 1,000 IU when necessary.

\*\* Can be taken up to 6-8 weeks.

\*\*\* If weekly dosage is preferred to daily dosage, a single dose of 50,000 IU can be used for up to 6-8 weeks. More than 50,000 IU of Vitamin D at once is not recommended.

The maximum dose should not exceed 1,000 IU/day in the use of medicines containing Vitamin D for the purpose of prophylaxis during pregnancy.

**Method of administration**

DEVIT-3 is taken orally with some water, and the capsules should be swallowed whole.

It is recommended that patients take DEVIT-3 with main meals (see section 5.2 Pharmacokinetic properties - “Absorption”).

**Additional information on special populations**

Certain populations are at greater risk of Vitamin D deficiency. Higher doses and serum 25(OH)D monitoring may be required:

- Institutionalized or hospitalized individuals
- Dark-skinned individuals
- Individuals with limited effective sun exposure due to protective clothing or consistent use of sun screens
- Obese individuals
- Patients being evaluated for osteoporosis
- Use of certain concomitant medications (e.g., anticonvulsant medications, glucocorticoids)
- Patients with malabsorption, including inflammatory bowel disease and coeliac disease

DEVIT-3 should not be given to children under 12 years of age due to the risk of suffocation.



Hepatic impairment

No data available.

Renal impairment

Due to the Vitamin D content of this medicine, it should not be used in concomitantly with calcium in patients with renal impairment.

Pediatric population

It is applied as stated in the section ‘Posology/frequency and duration of administration’.

Geriatric population

No data available.

**4.3 Contraindications**

- Hypersensitivity to cholecalciferol or other excipients in DEVIT-3
- Hypercalcemia and/or hypercalciuria
- Patients with nephrolithiasis or a tendency to produce calcium-containing kidney stones
- Severe renal impairment
- DEVIT-3 should not be used in children under 12 years of age due to the inability to swallow soft capsules and/or the potential for choking risk.
- Hypervitaminosis D

**4.4 Special warnings and precautions for use**

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.

Since cholecalciferol, the form of Vitamin D, cannot normally be metabolized in patients with severe renal impairment, other forms of Vitamin D should be used in those patients.

Caution is required in patients receiving treatment for cardiovascular disease (see section 4.5 Interaction with other medicinal products and other forms of interaction – cardiac glycosides including digitalis).

DEVIT-3 should be prescribed with caution to patients suffering from sarcoidosis because of the risk of increased metabolism of Vitamin D to its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Allowances should be made for the total dose of Vitamin D<sub>3</sub> in cases associated with treatments already containing Vitamin D<sub>3</sub>, foods enriched with Vitamin D<sub>3</sub>, cases using milk enriched with Vitamin D<sub>3</sub>, and the patient’s level of sun exposure.

There is no clear evidence for causation between Vitamin D<sub>3</sub> supplementation and renal stones, but the risk is plausible, especially in the context of concomitant calcium supplementation. The need for additional calcium supplementation should be considered for individual patients. Calcium supplements should be given under close medical supervision.

Oral administration of high-dose Vitamin D (500,000 IU by single annual bolus) was reported to result in an increased risk of fractures in elderly subjects, with the greatest increase occurring during



the first 3 months after dosing.

Vitamin D therapy may prevent the emergence of previously undiagnosed primary hyperparathyroidism. Adjusted serum calcium levels should be checked if suppressed primary hyperparathyroidism occurs 1 month after completion of the loading regimen or after initiation of Vitamin D supplementation. In addition, certain groups may be at increased risk of hypercalcemia with this treatment regimen and these individuals should be monitored by measuring their adjusted serum calcium levels.

DEVIT-3 should not be used in children under 12 years of age due to their inability to swallow capsules and/or the potential for choking risk.

Although the routine use of medicines containing Vitamin D during pregnancy is not recommended, they should be used under the supervision of a physician when necessary.

When using medicines containing Vitamin D for prophylaxis during pregnancy, the maximum dose should not exceed 1,000 IU/day.

Maximum tolerated dose for maintenance treatment and prophylaxis of risky groups (see section 4.2 Posology and method of administration):

Newborn: 1,000 IU/day (25 mcg/day)

1 month to 1 year: 1,500 IU/day (37.5 mcg/day)

1 year to 10 years: 2,000 IU / day (50 mcg/day)

11 years to 18 years: 4,000 IU / day (100 mcg/day)

Adults over 18 years of age: 4,000 IU/day (100 mcg/day)

DEVIT-3 contains sunset yellow, which may cause allergic reactions.

DEVIT-3 contains sorbitol. Patients with rare hereditary problems of fructose intolerance should not use this medicine.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

Concomitant use of anticonvulsants (such as phenytoin) or barbiturates (and possibly other medicines that induce hepatic enzymes) may reduce the effect of Vitamin D<sub>3</sub> by metabolic inactivation.

In cases of treatment with thiazide diuretics, which decrease urinary elimination of calcium, monitoring of serum calcium concentration is recommended.

Concomitant use of glucocorticoids can decrease the effect of Vitamin D<sub>3</sub>.

Patients receiving treatment with cardiac glycosides may be sensitive to elevated calcium levels. In these patients, electrocardiographic (ECG) parameters and calcium levels should be monitored. If the calcium in the urine exceeds 7.5 mmol/24 hours (300 mg/24 hours), dose reduction is recommended.

Simultaneous treatment with ion exchange resins such as cholestyramine, colestipol hydrochloride, orlistat or laxatives such as paraffin oil may reduce the gastrointestinal absorption of Vitamin D. Rifampicin may reduce the efficacy of cholecalciferol due to hepatic enzyme induction.

Because isoniazid inhibits the metabolic activation of cholecalciferol, it may reduce the efficacy of cholecalciferol.



Phosphate infusion should not be used to reduce hypercalcemia from Vitamin D hypervitaminosis because of the danger of metastatic calcification.

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.

Additional information on special populations

No data available.

Pediatric population

No data available.

**4.6 Pregnancy and lactation**

High-dose formulation is not recommended during pregnancy and lactation, therefore, lower doses of formulations should be used.

**General recommendation**

Pregnancy category is C.

**Women of child-bearing potential/Contraception**

Data on contraception are not available.

**Pregnancy**

There are no adequate data on the use of DEVIT-3 in pregnant women. Studies in animals have shown reproductive toxicity (see Section 5.3 Preclinical safety data). The potential risk to humans is unknown. When using medicines containing Vitamin D for prophylaxis during pregnancy, the maximum dose should not exceed 1,000 IU/day. The recommended daily intake for pregnant women is 400 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. Vitamin D<sub>3</sub> and its metabolites are excreted in breast milk.

Although the routine use of medicines containing Vitamin D during pregnancy is not recommended, they should be used under the supervision of a physician when necessary. These medicines should not be used during pregnancy unless absolutely necessary.

Based on human experience and animal experiments, Vitamin D overdose in pregnancy causes physical and mental impairment, congenital heart and eye problems due to hypercalcemia.

**Lactation**

Vitamin D can be prescribed while the patient is breast-feeding if necessary. This supplementation does not replace the administration of Vitamin D in the neonate.

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**



Data on the effects on fertility are not available.

#### **4.7 Effects on ability to drive and use machines**

No known effect. However, it seems unlikely to have any effect on this ability.

#### **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).

#### **Metabolism and nutrition disorders**

Uncommon: Hypercalcemia and hypercalciuria.

#### **Skin and subcutaneous disorders**

Rare: Pruritus, rash and urticaria.

#### Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization 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.

#### **4.9 Overdose**

Acute or chronic overdose of DEVIT-3 may increase the concentration of calcium in the urine and serum, resulting in hypercalcemia. Hypercalcemia symptoms are not very specific and in the initial stages they are often nausea, vomiting, diarrhea with subsequent constipation, anorexia, fatigue, headache, muscle and joint pain, muscle weakness, polydipsia, polyuria by kidney stones, nephrocalcinosis, renal failure, calcification of soft tissue, changes in ECG measurements, arrhythmia and pancreatitis. In rare and isolated cases, hypercalcemia has been reported to be fatal.

#### Treatment

Normalization of hypercalcemia due to Vitamin D intoxication takes several weeks. For the treatment of hypercalcemia, it is recommended to avoid supplements, foods, Vitamin D intake and sunlight. A low-calcium or no-calcium diet can be applied. Rehydration and treatment with diuretics, e.g. furosemide to ensure adequate diuresis. For additional treatment, calcitonin or corticosteroids may be given. To reduce the hypercalcemia caused by hypervitaminosis D, phosphate infusion should not be given because of the danger of metastatic calcification.

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

**Pharmacotherapeutic group:** Vitamin D and analogues, Cholecalciferol

**ATC code:** A11CC05

Cholecalciferol is produced in the skin following sunlight exposure. 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**

### **General specifications**

The pharmacokinetics of Vitamin D is well known.

#### Absorption

Vitamin D is well absorbed from the gastro-intestinal tract in the presence of bile, so the administration with the major meal of the day might therefore facilitate the absorption of Vitamin D.

#### Distribution

After a single dose of cholecalciferol maximum serum concentrations of the active metabolite 25-hydroxycholecalciferol are reached after about a week. The metabolites circulate in the blood bound to a specific  $\alpha$  – globin.

#### Biotransformation

It is hydroxylated in the liver to form 25-hydroxycholecalciferol and then undergoes further hydroxylation in the kidney to form the active metabolite 1,25 dihydroxy-colecalciferol (calcitriol).

#### Elimination

Vitamin D and its metabolites are excreted mainly in the bile and feces.

#### Linearity/Non-linearity

No studies available.

### **Characteristics in patients**

A 57% lower metabolic clearance rate is reported in subjects with renal impairment as compared with that of healthy volunteers.

Decreased absorption and increased elimination of Vitamin D occurs in subjects with malabsorption.

Obese subjects are less able to maintain Vitamin D levels with sun exposure, and are likely to require larger oral doses of Vitamin D to replace deficits.

## **5.3 Preclinical safety data**

Pre-clinical studies conducted in various animal species have demonstrated that toxic effects occur in animals at doses much higher than those required for therapeutic use in humans.

Cholecalciferol induced malformations in rats, mice, and rabbits at doses greater than human doses. These malformations include skeletal problems, microcephaly, and cardiac disorders.

In toxicity studies at repeated doses, the effects most commonly reported were increased calciuria and decreased phosphaturia and proteinuria.

Hypercalcemia has been reported in high doses. In a state of prolonged hypercalcemia, histological alterations (calcification) were more frequently borne by the kidneys, heart, aorta, testes, thymus and intestinal mucosa.

Colecalciferol has been shown to be teratogenic at high doses in animals.

At doses equivalent to those used therapeutically, colecalciferol has no teratogenic activity.



Colecalciferol has no potential mutagenic or carcinogenic activity.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Refined sunflower oil  
Gelatin  
Glycerin  
Sorbitol  
Deionized water

FD&C Yellow No:6  
Sunset Yellow FCF (E110)  
Sodium chloride

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf life**

24 months.

### **6.4 Special precautions for storage**

Store at room temperature below 25°C and in its original package.

### **6.5 Nature and contents of packaging**

As the primary packaging material of our DEVIT-3 20,000 IU Soft Capsules product, blisters consist of Opaque PVC/Aclar and aluminum foil.

Supplied with 2 blisters (7 capsules in each blister) 14 capsules in total, and a patient leaflet, all in a cardboard box.

### **6.6. Special precautions for disposal and other handling**

Any unused material should be disposed according to local disposal regulations.

## **7. MARKETING AUTHORIZATION HOLDER**

DEVA HOLDING A.Ş.  
Halkalı Merkez Mah. Basın Ekspres Cad. No.:1  
34303 Küçükçekmece - ISTANBUL/TURKEY

## **8. MARKETING AUTHORIZATION NUMBER(S)**

2022/428

## **9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION**

Date of first authorization : 04/08/2022  
Date of latest renewal :

## **10. DATE OF REVISION OF THE TEXT**

