SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DEVIT-3 10,000 IU Soft Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:
Cholecalciferol 10,000 IU
(Equivalent to 250 mcg Cholecalciferol)
Excipient(s) with known effect:
Sorbitol 6.72 mg
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Soft capsules.
Biconvex, oval, transparent, light yellow colored soft capsules.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

Posology/frequency and duration of administration
Each soft capsule contains 10,000 IU of cholecalciferol (vitamin D_3).

The doctor will decide how to use the medicine. It should be used according to the doctor's advice.

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 (1,250 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.*

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.

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.

Due to the risk of suffocation, this medicine should not be given to children under 12 years of age.

Method of administration
DEVIT-3 should be taken by mouth.
The capsules should be swallowed as whole with some water, preferably during a meal.
Patients should be advised to take this medicine preferably with a main meal (see section 5.2).

Additional information on special populations
Renal impairment
DEVIT-3 should not be used in patients with severe renal impairment.

Hepatic impairment
No data available.

Pediatric population
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.

Geriatric population
It should be administered as in adults.

4.3 Contraindications
- In patients with hypersensitivity to cholecalciferol or other excipients listed in section 6.1
- In patients with hypercalcemia and/or hypercalciuria
- In patients with nephrolithiasis (renal stones), nephrocalcinosis (too much calcium in the kidneys), or a tendency to produce calcium-containing renal stones (kidney stones)
- In patients with severe renal impairment
- DEVIT-3 should not be used in children under 12 years of age due to the inability to swallow the capsules and/or the potential for choking risk.
- In case of hypervitaminosis D

4.4 Special warnings and precautions for use
DEVIT-3 soft capsules should be used cautiously in patients with mild to moderate renal impairment 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).

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_3 in cases associated with treatments already containing Vitamin D_3, foods enriched with Vitamin D_3, cases using milk enriched with Vitamin D_3, and the patient's level of sun exposure.

During long-term treatment with an equivalent daily dose exceeding 1,000 IU vitamin D, the serum calcium values must be monitored. Renal function should also be checked by measuring serum creatinine. It is recommended to reduce the dose or interrupt treatment if the calcium content in the urine exceeds 7.5 mmol / 24 hours (300 mg / 24 hours).

There is no clear evidence for causation between Vitamin D_3 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.

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.

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

Pediatric population
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.

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_3 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_3.

In cases of treatment with drugs containing digitalis and other cardiac glycosides, the administration of Vitamin D_3 may increase the risk of digitalis toxicity (arrhythmia). Strict medical supervision is needed, together with serum calcium concentration and electrocardiographic monitoring if necessary.

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.

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.

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 or limited data on the use of cholecalciferol in pregnant women. Studies in animals have shown reproductive toxicity (see section 5.3). 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_3 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.

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

DEVIT-3 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
Cholecalciferol and its metabolites are excreted in breast milk. High strength formulations are not recommended in 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.
In addition, there is a risk of hypercalcemia in infants of nursing mothers who receive pharmacological doses of Vitamin D.

Fertility
There is no data regarding treatment with Vitamin D_3 and its effects on fertility.

4.7 Effects on ability to drive and use machines
There are no data on the effects of DEVIT-3 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: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥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
Discontinue DEVIT-3 when calcemia exceeds 10.6 mg/dL (2.65 mmol/L) or if the calciuria exceeds 300 mg/24 hours in adults or 4-6 mg/kg/day in children. Overdose manifests as hypercalcemia and hypercalciuria, the symptoms of which include: nausea, vomiting, thirst, constipation, polyuria, polydipsia, and dehydration.

Chronic overdosage may lead to vascular and organ calcification, as a result of hypercalcemia.

Treatment
DEVIT-3 administration should be terminated and rehydration should be initiated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Vitamin D and analogues, Cholecalciferol
ATC code: A11CC05

Mechanism of action
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 Vitamin D_3. PTH secretion is inhibited additionally by the increased calcium uptake in the small intestine under the influence of biologically active Vitamin D.

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 and biotransformation

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

Elimination

The metabolites circulate in the blood bound to a specific α – globin, Vitamin D and its metabolites are excreted mainly in the bile and feces. Small amounts of Vitamin D can be found in the urine.

Characteristics in Specific Groups of Subjects or 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. 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

Sunflower oil
Gelatin
Glycerin
Sorbitol
Deionized water

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 10,000 IU Soft Capsules product, blisters consist of Opaque PVC/Aclar and aluminum foil.
Supplied with 3 blisters (10 capsules in each blister) 30 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)

2021/81

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization : 27/03/2021
Date of latest renewal :

10. DATE OF REVISION OF THE TEXT