SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

DEVIT-3 2,000 IU Soft Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each soft capsule contains:
Active Substance:
Cholecalciferol……......2,000 IU
(Equivalent to 50 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, matte red 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 2,000 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.

Method of administration
DEVIT-3 should be taken by mouth.
The capsules should be swallowed as whole with some water.

Additional information on special populations
Renal impairment
It should not be used in patients with severe renal impairment (see section 4.3).

Hepatic impairment
No dose adjustment is required.

Pediatric population
It should be applied as stated in the section ‘‘Posology/frequency and duration of administration’’.
It is not intended for use in children under 12 years of age.

Geriatric population
It should be administered as in adults.

4.3 Contraindications
- In patients with hypersensitivity to the active substance (cholecalciferol) or other excipients listed in section 6.1
- In diseases and/or conditions resulting in hypercalcemia and/or hypercalciuria,
- In case of nephrolithiasis (kidney stone),
- In case of nephrocalcinosis (ectopic deposit of calcium salts in the renal parenchyma, renal calcification),
- In case of hypervitaminosis D.
- In patients with severe renal impairment,
- In children under 12 years of age,

4.4 Special warnings and precautions for use
DEVIT-3 should be prescribed with caution to patients suffering from sarcoidosis, a disease caused by abnormal functioning of the immune system, 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.

Caution is required in patients receiving treatment for cardiovascular disease (see section 4.5).

During long-term treatment, the serum calcium values must be monitored and renal function should also be checked by measuring serum creatinine. Follow-up is essential especially in the elderly patients undergoing concomitant therapy with cardiac glycosides or diuretics (see section 4.5) and in patients with a high predisposition to form renal stones. Dose reduction or treatment interruption is required in case of hypercalciuria at levels exceeding 300 mg / 24 hours (7.5 mmol / 24 hours) or signs of renal dysfunction.

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.

The vitamin D content (2,000 IU) in DEVIT-3 should be considered when prescribing other medicinal products containing vitamin D. Additional doses of vitamin D should be taken under close medical supervision. In such cases, frequent monitoring of serum calcium levels and urinary calcium excretion is necessary.

The need for additional calcium supplementation should be considered for individual patients. Calcium supplements should be given under close medical supervision. In such cases, frequent monitoring of serum calcium levels and urinary calcium excretion is necessary.

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.

4.5 Interaction with other medicinal products and other forms of interaction
Phosphate infusions should not be administered to lower hypercalcemia of hypervitaminosis D because of the dangers of metastatic calcification.

Simultaneous administration of thiazide diuretics increases the risk of hypercalcemia because they decrease the calcium excretion in the urine. Therefore, serum and urine calcium levels should be monitored regularly during concomitant use of thiazide diuretics.

Concomitant treatment with phenytoin and barbiturates can decrease the effect of vitamin D as it increases the metabolic rate.

Excessive dosing of vitamin D with digitalis or other cardiac glycosides may induce hypercalcemia, 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 monitored closely.

Glucocorticoid steroids can increase the rate of metabolism and elimination of vitamin D. During concomitant use with glucocorticoid steroids, the dose of DEVIT-3 capsules may need to be increased.

Rifampicin may reduce the effectiveness of cholecalciferol due to hepatic enzyme induction.

Isoniazid may reduce the effectiveness of cholecalciferol due to inhibition of the metabolic activation of cholecalciferol.

Simultaneous treatment with ion exchange resins such as cholestyramine, colestipol, or laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D. Orlistat may potentially impair the absorption of cholecalciferol, as it causes fat malabsorption.

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
General recommendation
Pregnancy category is C.

Women of child-bearing potential/Contraception
Data on contraception are not available.

Pregnancy
High-dose vitamin D has teratogenic effects in animal experiments. Overdose of vitamin D should be avoided during pregnancy because prolonged hypercalcemia causes physical and mental disorders (mental retardation), supravalvular aortic stenosis and eye disorders.

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.

Studies in animals have shown reproductive toxicity (see section 5.3). The potential risk to humans is unknown. DEVIT-3 should not be used during pregnancy unless absolutely necessary.

Lactation
Vitamin D and its metabolites are excreted in breast milk. No overdose cases have been observed in infants induced by nursing mothers taking cholecalciferol; 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
No data on the effect of DEVIT-3 on fertility are available. Normal endogenous levels of vitamin D are not expected to produce any adverse effects on fertility.

4.7 Effects on ability to drive and use machines
No studies on the effects on the ability to drive or use machines have been performed. However, DEVIT-3 has no known side effects that are likely to affect the ability to drive and use or operate machines.

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).

Immune system disorders
Not known: Hypersensitivity reactions such as angioedema, and laryngeal edema.

Metabolism and nutrition disorders
Uncommon: Hypercalcemia, hypercalciuria.

Skin and subcutaneous disorders
Rare: Pruritus, rash, 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
Overdose can lead to hypervitaminosis D. An excess of vitamin D causes abnormally high levels of calcium in the blood, which can eventually cause serious damage to the soft tissues and kidneys.

Acute or chronic overdose of cholecalciferol may increase the concentration of calcium in the urine and serum, resulting in hypercalcemia. Symptoms of hypercalcemia (increased concentrations of calcium in the serum and urine) include anorexia, thirst, nausea, vomiting, diarrhea often in the early stages and later constipation, abdominal pain, muscle weakness, fatigue, mental disorders, polydipsia, polyuria, pain in the bones, nephrocalcinosis. In severe cases, symptoms are renal stones, renal failure, calcification of soft tissues, changes in ECG measurements, pancreatitis, and cardiac arrhythmias. Severe hypercalcemia can result in coma and death.

High levels of calcium in the blood can cause permanent and irreversible renal damage and soft tissue calcification.

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.

Treatment of hypercalcemia:
Vitamin D treatment should be discontinued. However, treatment with thiazide diuretics, lithium, vitamin A and cardiac glycosides should also be discontinued. Depending on rehydration and severity, treatment with loop diuretics, bisphosphonates, calcitonin, and corticosteroids should be considered, either alone or in combination. In addition, patients' serum electrolytes, renal functions and diuresis should be monitored. In severe cases, ECG and CVP should be monitored.

Phosphate infusions should not be administered to lower hypercalcemia of hypervitaminosis D because of the dangers of metastatic calcification.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

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

Vitamin D increases the absorption of calcium and phosphate in the intestine.

Vitamin D_3 administration prevents the development of rickets in children and osteomalacia in adults. It also prevents the increase of parathyroid hormone (PTH), which is caused by calcium deficiency and causes increased bone resorption.

In addition to bone and intestinal mucosa, many other tissues contain vitamin D receptors that bind calcitriol, the active hormonal form of vitamin D.

5.2 Pharmacokinetic properties

General specifications

Vitamin D

Exposure to sunlight: 7-dehydrocholesterol, found in the skin, is converted to cholecalciferol by UVB light.

Absorption

Cholecalciferol is well absorbed from the gastro-intestinal tract. Taking vitamin D with food potentially increases its absorption.

Distribution

Cholecalciferol and its metabolites circulate in the blood bound to a specific globin.

Biotransformation

Cholecalciferol is hydroxylated in the liver to form 25-hydroxy-colecalciferol ($25(OH)D_3$, calcidiol) and then undergoes further hydroxylation in the kidneys to form 1,25-dihydroxy-colecalciferol (calcitriol), the active metabolite of cholecalciferol, responsible for increasing calcium absorption. If not metabolized, vitamin D is stored in fat and muscle tissues.

Elimination

After a single oral dose of cholecalciferol, the maximum serum concentrations of the primary storage form are reached after approximately 7 days. $25(OH)D_3$ is then slowly eliminated with an apparent half-life in serum of about 50 days. Cholecalciferol and its metabolites are excreted mainly in the bile and faces. Small amounts of Vitamin D can be found in the urine.

5.3 Preclinical safety data

Teratogenicity has been observed in animal studies at doses much higher than the human therapeutic dose range. No further specific data that are not mentioned in other sections of the SPC (see sections 4.6 and 4.9) are available.
Colecalciferol overdosage in animals has been shown to induce malformations in rats, mice, and rabbits at doses significantly greater than human doses. These malformations include skeletal defects, microcephaly, and cardiac malformations.
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
Iron oxide red

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 DEVIT-3 2,000 IU Soft Capsules, blisters consist of Opaque PVC/Aclar and aluminum foil.
Supplied with 6 blisters (10 capsules in each blister) of 60 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)

2022/430

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