Devit 50 000 Tablets film-coated

Summary of Product Characteristics

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1. Name of the Medicinal Product
Devit 50 000

2. Qualitative and Quantitative Composition
Each film-coated tablet contains 50 000 IU of Vitamin D3 (equivalent to 1.25mg of cholecalciferol)

3. Pharmaceutical Form
Tablets film-coated

4. Clinical Particulars

4.1 Therapeutic indications
Treatment of Vitamin D deficiency
Prophylaxis of vitamin D deficiency in high-risk patients and patients with increased vitamin D needs.

4.2 Posology and method of administration
Patients with high risk of vitamin D deficiency and conditions of increased vitamin D needs:
Osteomalacia
Osteoporosis
Unbalanced diet (including vegetarian diet and parenteral nutrition)
Malabsorption problem
Insufficient solar exposure
Hypocalcaemia
Hypophosphatemia (including heredetary)
Alcohol addiction
Hepatic insufficiency
Cirrhosis
Obstructive jaundice
Illnesses of gastroenteric tract (celiac disease, persistent diarrhea, tropical diarrhea, Crohn's disease)
Quick weight loss
Intake of barbiturates, colestyramine, colestipol, mineral oils, seizure medications (e.g. phenytoin, primidone), glucocorticoids.

For Vitamin D deficiency treatment: serum levels of 25-(OH) D < 25 nmol/l or <10 ng/ml for adults and elderly:

- 50 000 IU/Week (1 tablet), 8 weeks followed by maintenance treatment (equivalent to 1400-2000 IU/day), e.g. 1 tablet/month if required.
- 200 000 IU/month (4 tablets), 2 months followed by maintenance treatment (equivalent to 1400-2000 IU/day), e.g. 1 tablet/month if required.
- 150 000 IU/month (3 tablets), 3 months followed by maintenance treatment (equivalent to 1400-2000 IU/day), e.g. 1 tablet/month if required.

For Vitamin D insufficiency treatment: serum levels of 25-(OH) D 25-50 nmol/l or 10-20 ng/ml for adults and elderly

- 50 000 IU/Week (1 tablet), 4 weeks followed by maintenance treatment (equivalent to 1400-2000 IU/day), e.g. 1 tablet/month if required.

- 200 000 IU/month (4 tablets), 1 month followed by maintenance treatment (equivalent to 1400-2000 IU/day), e.g. 1 tablet/month if required
- 150 000 IU/month (3 tablets), 1 month followed by maintenance treatment (equivalent to 1400-2000 IU/day), e.g. 1 tablet/month if required

Maintenance treatment is done with 25-(OH) D concentration in blood control: 1 tablet/month during 3-4 months or 1 tablet per 2 weeks during 3-4 months (for individuals suffering from obesity or vitamin D dysmetabolism. Dosage is chosen individually depending from severity of vitamin D deficiency and response to treatment.

For Vitamin D deficiency treatment: serum levels of 25-(OH) D < 25 nmol/l or <10 ng/ml for *adolescents 12-18 years old*:

- 50 000 IU/Week (1 tablet), 8 weeks followed by maintenance treatment (equivalent to 1400-2000 IU/day), e.g. 1 tablet/month if required

For Vitamin D insufficiency treatment: serum levels of 25-(OH) D 25-50 nmol/l or 10-20 ng/ml for *adolescents 12-18 years old:*

- 50 000 IU/Week (1 tablet), 4 weeks followed by maintenance treatment (equivalent to 1400-2000 IU/day), e.g. 1 tablet/month if required

Maintenance treatment is done with 25-(OH) D concentration in blood control: 1 tablet/month during 3-4 months. Dosage is chosen individually depending from severity of vitamin D deficiency and response to treatment.

Method of administration
Oral. The film-coated tablet should be swallowed whole (not chewed) with water independently of meals.

Before starting vitamin D treatment, assess blood calcium and phosphate levels. For treatment to be effective, adequate dietary calcium intake must be ensured.
Due to variation in individual sensitivity to vitamin D, dosage may be adjusted based on clinical efficacy.
When choosing a dose for D, it is necessary to take into account the amount of its consumption from other sources.
In patients on hemodialysis, phosphate binders (phosphate binders) may be used to control elevated plasma phosphate levels. During vitamin D therapy, an increase in the dose of phosphate binders may be required due to the improvement in phosphate absorption. Plasma product of calcium and phosphorus (Ca × P, mg / dL) should not exceed 60.
The administration of high doses of vitamin D to pregnant women and breastfeeding is not recommended due to the possible teratogenic effects. This high dose vitamin D drug is contraindicated in these patients. If it is necessary to prescribe vitamin D to this category of patients, other, significantly lower dosages of the drug should be used.

Vitamin D deficiency in the body with malabsorption or liver disease often requires higher doses for treatment, up to 1 mg (40,000 IU) daily. Doses up to 2.5 mg (100,000 IU) can be used to treat hypocalcemia due to hypoparathyroidism.

Patient monitoring
With long-term use of high doses (at the rate of 10,000 IU per day), monitoring of the following indicators is recommended.

- Blood calcium concentration or plasma ionized calcium level. Due to the narrow therapeutic range, it is recommended to determine these indicators at least once a week in the early period of treatment, then periodically during treatment. If possible, it is worth determining the concentration of both free and bound calcium in the blood.
- The level of alkaline (alkaline) phosphatase in the blood plasma, the concentration of phosphates in the blood, the concentration of calcium in the 24-hour urine, the ratio of calcium and creatinine in the urine. It is recommended to determine these indicators every 1-3 months during therapy.
- Plasma urea nitrogen and plasma creatinine. Periodic testing is recommended in patients receiving therapeutic doses.

Special patient groups:
Children
DeVit 50,000 is not recommended for children under 12 years of age due to the lack of the ability of many to safely swallow a pill.

Elderly patients
Studies show that elderly patients may have an increased need for vitamin D due to a decrease in the skin's ability to synthesize previtamin D3, or a decrease in sun exposure, or a weakened renal function, or a weakened absorption of vitamin D. in blood plasma.

Patients with impaired liver function
Deficiency of vitamin D in the body in liver disease often requires higher doses for treatment. To select a dosage, it is necessary to focus on the concentration of 25-hydroxycholecalciferol in the blood plasma.

4.3 Contraindications
- Hypersensitivity to vitamin D or any of the excipients in the product.
- Hypervitaminosis D.
- Renal osteodystrophy with hyperphosphatemia.
- Diseases or conditions resulting in hypercalcemia and/or hypercalciuria.

With special care:
- Urinary stone disease, risk of calcium stones development in kidney.
- Severe renal failure.
- Kids younger than 12 years old.
- Pregnancy. Prescription of high doses is not recommended and if required the use of smaller doses is preferable.

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. In patients with severe renal insufficiency, vitamin D in the form of cholecalciferol is not metabolized normally and other forms of vitamin D should be used (see

section 4.3, contraindications). Caution is required in patients receiving treatment for cardiovascular disease (see Section 4.5 - cardiac glycosides including digitalis).
Devit 50 000 i.u 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 vitamin D supplements from other sources.
The need for additional calcium supplementation should be considered for individual patients. Calcium supplements should be given under close medical supervision.
Medical supervision is required whilst on treatment to prevent hypercalcaemia.
Peroral intake of high dosage vitamin D (e.g. 500 000 IU bolus dose) may increase the risk of fractures in elderly
Treatment with vitamin D may reveal primary hyperparathyroidism. Serum blood calcium levels should be checked after 1 month of loading regime or after addition of vitamin D.
If hypercalciuria is detected (higher than 300 mg or 7.5 mmol/24 hours) or in case of hepatic impairment the treatment must be abandoned. Similar control should be done for kids whose mothers received treatment with vitamin D in pharmacological dosages. Some children may have higher sensibility to vitamin D action.
Devit tablets should not be applied in case of pseudohypoparathyroidism (vitamin D demand may be decreased). Other vitamin D derivatives may be used in this case.

4.5 Interaction with other medicinal products and other forms of interaction
Concomitant treatment with phenytoin, hydantoin, primidon or barbiturates can decrease the effect of vitamin D because of metabolic activation. Concomitant use of glucocorticoids can decrease the effect of vitamin D. Systemic corticosteroids suppress calcium absorption. Prolonged corticosteroids intake may be optimized by vitamin D action.
The effects of digitalis and other cardiac glycosides may be accentuated with the oral administration of calcium combined with Vitamin D. Strict medical supervision is needed and, if necessary monitoring of ECG and calcium.
Simultaneous treatment with ion-exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D.
Thiazide diuretics interact with Vitamin D. Vitamin D helps the body absorb calcium. The thiazide diuretics increase the amount of calcium in the body. Taking large amounts of Vitamin D along with diuretics might cause too much calcium in the body. Calcium level monitoring is advised.
Cytotoxic agent actinomycin and antifungal imidazole agents act with vitamin D and inhibit transformation of 25-hydroxyvitamin D into 1.25-dihydroxyvitamin D under action of kidney enzyme (25-hydroxyvitamin D-1-hydroxylase).
Intake of calcium containing products at high dosages may increase the risk of hypercalcemia.
It is advised to avoid products containing magnesium (e.g. antacids) due to a higher risk of hypermagnesemia. Vitamin D increases the absorption of phosphorus containing drugs and consequently the risk of hyperphosphatemia.
Simultaneous intake of calcitonin, etidronate, gallium nitrate, pamidronate, plicamycin with vitamin D may antagonize the effect of this drug products while hypercalcemia treatment.

4.6 Pregnancy and lactation

There are no or limited amount of data from 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 the treatment.

Pregnancy

Problems in humans have not been documented with intake of normal daily requirements. Maternal hypercalcaemia during pregnancy in humans may be associated with increased sensitivity to effects of vitamin D, suppression of parathyroid function, or a syndrome of peculiar (elfin) facies, mental retardation and congenital aortic stenosis in infants.

Lactation

Only small amounts of vitamin D metabolites appear in human milk. Infants who are totally breast-fed and have little exposure to the sun may require vitamin D supplementation. Vitamin D should not be administered to patients with hypercalcaemia. It should be administered with caution to infants as they may have increased sensitivity to its effects and should be used with care in patients with renal impairment or calculi, or heart disease, who might be at increased risk of organ damage if hypercalcaemia occurred. Plasma phosphate concentrations should be controlled during vitamin D therapy to reduce the risk of ectopic calcification.

It is advised that patients receiving pharmacological doses of vitamin D should have their plasma-calcium concentration monitored at regular intervals, especially initially and if symptoms suggest toxicity similar monitoring is recommended in infants if they are breast fed by mothers receiving vitamin D. Growth may be arrested in children, especially after prolonged administration of 45mcg (1800 units) of cholecalciferol a day.

Effects on ability to drive and use machines

Devit 50 000i.u has no influence on the ability to drive and use machines.

4.7 Effects on ability to drive and use machines:

There is no available data concerning the negative effect of the product on the ability to drive and use machines.

4.8 Undesirable effects

Like all medicines Devit 50 000 can cause side effects, although not everybody gets them. Side effects with Devit 50 000 may include:

Uncommon side effects (affecting less than 1 in 100 people):

- too much calcium in the blood (hypercalcaemia). You may feel or be sick, lose your appetite, have constipation, stomach ache, feel very thirsty, have muscle weakness, drowsiness or confusion.
- too much calcium in your urine (hypercalciuria)

Rare side effects (affecting less than 1 in 1000 people):

- Skin rash, itching, hives, face oedema, genital oedema, dry skin, nail disorder, dry mouth, loss of appetite, erythematosus rash, purpuric rash, choking, and dysphagia.

Growth may be arrested in children, especially after prolonged administration of 45mcg (1800 units) of cholecalciferol per day.
Early symptoms of vitamin D toxicity associated with hypercalcaemia Constipation - usually more frequent in children and adolescents; diarrhea; dryness of mouth; headache, continuing; increased thirst; increase in frequency of urination, especially at night, or in amount of urine; loss of appetite; metallic taste; nausea or vomiting - usually more frequent in children and adolescents; unusual tiredness or weakness.
Late symptoms of vitamin D toxicity associated with hypercalcaemia: bone pain; cloudy urine; high blood pressure; increased sensitivity of eyes to light or irritation of eyes; irregular heartbeat; itching of skin; lethargy (drowsiness); muscle pain; nausea or vomiting and pancreatitis (stomach pain, severe); psychosis, overt (mood or mental changes); weight loss.
Stop taking Devit if you experience serious side effects such as thinking problems, changes in behavior, feeling irritable, urinating more than usual, chest pain, feeling short of breath, or early signs of vitamin D overdose (weakness, metallic taste in mouth, weight loss, muscle or bone pain, constipation, nausea, and vomiting).

4.9 Overdose

Excessive intake of vitamin D leads to the development of hypercalcaemia and its associated effects including hypercalciuria, ectopic calcification, and renal and cardiovascular damage. Symptoms of overdose include anorexia, lassitude, nausea and vomiting, diarrhea, polyuria, sweating, headache, thirst and vertigo. Interindividual tolerance to vitamin D varies considerably; infants and children are generally more susceptible to its toxic effects. Recommended treatment includes the following:
Hypervitaminosis D is treated by withdrawal of the vitamins, low-calcium diet, and generous fluid intake. If hypercalcaemia persists, a low-calcium diet and prednisone may be started. Severe hypercalcaemia may be treated with calcitonin, etidronate, pamidronate, or gallium nitrate. Hypercalcemia crisis requires vigorous hydration with intravenous saline to increase calcium excretion, with or without a loop diuretic. Cardiac arrhythmias may be treated with small doses of potassium with continuous cardiac monitoring.
Seek medical attention if you think you have used too much of this medicine. An overdose of Vitamin D can cause serious or life-threatening side effects.

5. Pharmacological Properties

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Vitamin D and analogues
ATC code: A11CC05
Vitamin D3 regulates the exchange of calcium and phosphorus in the body, accelerates the absorption of calcium in the intestine, improves the reabsorption of calcium and phosphorus in the kidneys, maintains the required level of these elements in the blood, promotes the formation of the bone skeleton, as well as the preservation of bone structure.

The concentration of calcium ions in the blood causes the maintenance of muscle tone of the skeletal muscles, myocardial function, promotes the conduction of nervous excitement, and regulates the process of blood coagulation.
Also, vitamin D3 is necessary for the normal functioning of the parathyroid glands.
With aging, sun exposure and the ability of the skin to synthesize vitamin D3 decrease. Due to the weakening of kidney function, the level of the active metabolite of vitamin D, 1.25 (OH) 2D, produced in the kidneys, decreases, which contributes to the widespread prevalence of vitamin D deficiency among the elderly.
Since vitamin D is required for adequate calcium absorption and normal bone metabolism, chronic vitamin D deficiency causes secondary hyperparathyroidism and, as a consequence, activation of bone metabolism and rapid bone loss. Vitamin D supplementation, especially when combined with calcium supplementation, has been shown to slow bone loss and reduce the incidence of fractures.
Vitamin D therapy is a mandatory component of osteoporosis prevention along with calcium intake. In addition, taking vitamin D is an essential component of the complex treatment of established osteoporosis.

5.2 Pharmacokinetic properties
The pharmacokinetics of vitamin D are well understood.
Vitamin D is well absorbed (in the small intestine) from the gastrointestinal tract in the presence of bile (by 60-90%, with hypovitaminosis, almost completely). It is hydroxylated in the liver to form 25-hydroxycholecalciferol, and then undergoes further hydroxylation in the kidneys to form the active metabolite of 1,25-hydroxycholecalciferol (calcitriol). These metabolites circulate in the blood, plasma and lymphatic system by binding to specific alpha globulin. It circulates in the form of chylomicrons and lipoproteins.
It accumulates in large quantities in bones, in lesser amounts - in the liver, muscles, blood, small intestine, it remains especially long in adipose tissue. In small quantities it passes into breast milk. Vitamin D and its metabolites are excreted from the body, mainly with bile and feces, in small amounts by the kidneys. Cumulates.
An increase in Ca2 + in the blood begins 12-24 hours after taking the drug, the therapeutic effect is noted after 10-14 days and lasts up to 6 months.
Features of the pharmacokinetics of the drug in some groups of patients.
In patients with impaired renal function, a 57% decrease in the rate of metabolic clearance was observed compared with the same indicator in healthy volunteers.
In volunteers with malabsorption syndrome, a decrease in absorption and an acceleration of excretion of vitamin D was observed.
Obese volunteers are less able to maintain vitamin D levels when exposed to the sun, and therefore higher doses are required.

5.3 Preclinical safety data
Vitamin D is well known and is a widely used material and has been used in clinical practice for many years. As such toxicity is only likely to occur in chronic overdose where hypercalcaemia could result.

Cholecalciferol has been shown to be teratogenic in high doses in animals (4-15 times the human dose). Offspring from pregnant rabbits treated with high doses of vitamin D had lesions anatomically similar to those of supravalvular aortic stenosis and offspring not showing such changes show vasculotoxicity similar to that of adults following acute vitamin D toxicity.

6. Pharmaceutical Particulars

6.1 List of excipients

Microrystalline cellulose PH102:290, Precipitated silicon dioxide, Di-calcium phosphate anhydrous, Magnesium stearate, Croscarmellose sodium

Coating

Sepifilm LP 014 clear (Hydroxypropyl methylcellulose, Microcrystalline cellulose, Stearic Acid), Sepisperse Dry 5047 red (Hydroxypropyl methylcellulose, Microcrystalline cellulose, Titanum dioxide E171, Iron oxide red E 172)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store in a dry place below 30° C.

6.5 Nature and contents of container
8 or 15 film-coated tablets in PVC/Aluminium blister. 1 blister per package.

6.6. Instructions for use and handling
No special requirements.

7. Manufacturer
Quest Vitamins Middle East Fze, Dubai, U.A.E.
Dubai, U.A.E., Jebel-Ali Free Zone, Plot S20708A - to Lamyra LLP order, United Kingdom.

8. Marketing Authorization Holder
Quest Vitamins Middle East Fze, Dubai, U.A.E.
Dubai, U.A.E., Jebel-Ali Free Zone, Plot S20708A.

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