SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Divifarm 2000 IU film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains cholecalciferol (vitamin D_3) 2000 IU (equivalent to 50 microgram vitamin D_3).

Excipients with known effect
Each film-coated tablet contains 141 mg lactose (as lactose monohydrate) and 4 mg sucrose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

<invented name> 2000 IU: yellow coloured, round, 9 mm diameter biconvex film-coated tablets, embossed ‘S’ on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of vitamin D deficiency in adults and adolescents aged 12 years and older.
Vitamin D deficiency is defined as serum levels of 25-hydroxycolecalciferol (25(OH)D) < 25 nmol/l.

4.2 Posology and method of administration

The dosage must be determined individually by the treating doctor, depending on the extent of the necessary vitamin D_3 supplementation.

Posology
One tablet per day.
The dose should be adjusted dependent upon desirable serum levels of 25-hydroxycolecalciferol (25(OH)D), the severity of the disease and the patient´s response to treatment.

The daily dose should not exceed 4000 IU (two tablets per day).

After the first month, a lower maintenance dose should be considered dependent upon desirable serum levels of 25-hydroxycholecalciferol (25(OH)D), the severity of the disease and the patient´s response to treatment.

Paediatric population
The safety and efficacy of <invented name> in children under 12 years have not been established.

Dosage in hepatic impairment
No dose adjustment is required.

Dosage in renal impairment
In severe renal impairment the dosage must be determined individually by the treating physician dependent upon desirable serum levels of 25-hydroxycholecalciferol (25(OH)D), the severity of the disease and the patient´s response to treatment (see section 4.4).

Method of administration
The tablets can be swallowed whole or crushed. The tablets can be taken with food.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Diseases and/or conditions resulting in hypercalcaemia or hypercalciuria
- Nephrolithiasis
- Nephrocalcinosis
- Hypervitaminosis D

4.4 Special warnings and precautions for use

Monitoring
During treatment, serum and urinary calcium levels should be followed and renal function should be monitored through measurements of serum creatinine. Monitoring is especially important in elderly patients on concomitant treatment with cardiac glycosides or diuretics (see section 4.5) and in patients with a high tendency to calculus formation. In case of hypercalciuria (exceeding 300 mg (7.5 mmol)/24 hours) or signs of impaired renal function the dose should be reduced or the treatment discontinued.

Sarcoidosis
Vitamin D_3 should be prescribed with caution to patients suffering from sarcoidosis due to risk of increased metabolism of vitamin D into its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Renal impairment
Vitamin D_3 should be used with caution in patients with renal impairment 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 impairment, vitamin D in the form of cholecalciferol is not metabolised normally (see section 4.2).

Other vitamin D_3 containing products
The content of vitamin D (2000 IU) in this medicinal product should be considered when prescribing other medicinal products containing vitamin D. Additional doses of vitamin D should be taken under close medical supervision.

Excipients
This medicinal product contains lactose and sucrose.
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption and patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicinal product.

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Thiazide diuretics
Thiazide diuretics reduce the urinary excretion of calcium. Due to the increased risk of hypercalcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics.

Phenytoin and barbiturates
Concomitant use of phenytoin or barbiturates may reduce the effect of vitamin D since the metabolism increases.

Digitalis
Excessive dosing of vitamin D can induce hypercalcaemia, 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 closely monitored.

Glucocorticoids
Glucocorticoid steroids may increase vitamin D metabolism and elimination. During concomitant use, it may be necessary to increase the dose of <invented name> tablets.

Orlistat, ion exchange resins and laxatives
Simultaneous treatment with orlistat or ion exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D.

4.6 Fertility, pregnancy and lactation

Pregnancy
Overdoses of vitamin D have been shown to have teratogenic effects in animal experiments (see section 5.3). There are no indications that vitamin D at therapeutic doses is teratogenic in humans. Colecalciferol should be used during pregnancy only in the case of a vitamin D deficiency. Colecalciferol is not recommended during pregnancy in patients without a vitamin D deficiency.

Breastfeeding
Vitamin D_3 and its metabolites are excreted in breast milk. No adverse events have been observed in infants. <invented name> can be used at recommended doses during lactation in case of a vitamin D deficiency. 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 effects on fertility.

4.7 Effects on ability to drive and use machines

<invented name> has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions frequencies are defined as: uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000) or not known (cannot be estimated from the available data).

Immune system disorders
Not known: Hypersensitivity reactions such as angioedema or laryngeal oedema.

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia and hypercalciuria.

Skin and subcutaneous tissue disorders
Rare: Pruritus, rash and urticaria.

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

Overdose can lead to hypervitaminosis D. An excess of vitamin D causes abnormally high levels of calcium in the blood.

Symptoms of hypercalcaemia may include anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, mental disturbances, polydipsia, polyuria, bone pain, nephrocalcinosis, renal calculi and in severe cases, cardiac arrhythmias. Extreme hypercalcaemia may result in coma and death. Persistently high calcium levels may lead to irreversible renal damage and soft tissue calcification.
Treatment of hypercalcaemia: The treatment with vitamin D must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A, and cardiac glycosides must also be discontinued. Rehydration, and, according to severity, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids should be considered. Serum electrolytes, renal function and diuresis must be monitored. In severe cases, ECG and CVP should be followed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Vitamin D and analogues, cholecalciferol
ATC code: A11C C05

Vitamin D increases the intestinal absorption of calcium and phosphate.
Administration of vitamin D_3 counteracts development of rickets in children and osteomalacia in adults. It also counteracts the increase of parathyroid hormone (PTH) which is caused by calcium deficiency and which causes increased bone resorption.
In addition to bone and intestinal mucosa many other tissues have vitamin D receptors, to which the active hormonal form of vitamin D, calcitriol, binds.

5.2 Pharmacokinetic properties

Vitamin D
Absorption
Vitamin D is easily absorbed in the small intestine.

Distribution
Cholecalciferol and its metabolites circulate in the blood bound to a specific globulin. Vitamin D, which is not metabolised, is stored in adipose and muscle tissues.

Metabolism
Cholecalciferol is converted in the liver by hydroxylation to 25-hydroxycholecalciferol. It is then further converted in the kidneys to 1.25- dihydroxycholecalciferol. 1.25-dihydroxycholecalciferol is the active metabolite responsible for increasing calcium absorption.

Elimination
Vitamin D is excreted in faeces and urine.

5.3 Preclinical safety data

At doses far higher than the human therapeutic range teratogenicity has been observed in animal studies. There is no further information of relevance to the safety assessment in addition to what is stated in other parts of the SPC.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
lactose monohydrate
powdered cellulose (E460 (ii))
modified food starch
maize starch
croscarmellose sodium (E468)
sucrose
colloidal anhydrous silica (E551)
magnesium stearate (E470b)
sodium ascorbate (E301)
medium chain triglycerides
All-rac-alpha-tocopherol (E307)

Coating:
polyvinyl alcohol (E1203)
titanium dioxide (E171)
macrogol 3350
talc (E553b)
quinoline yellow aluminum lake (E104)
yellow iron oxide (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 25^{o}C.

Keep the blister in the outer carton in order to protect from light.

6.5 Nature and contents of container

<invented name> 2000 IU film-coated tablets: 90 and 100 film-coated tablets in opaque PVC/PVdC-Alu blisters and box.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal <and other handling>

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

<To be completed nationally>

8. MARKETING AUTHORISATION NUMBER(S)

<[To be completed nationally]>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<[To be completed nationally]>

10. DATE OF REVISION OF THE TEXT

2025-06-12