

## Summary of Product Characteristics

### 1 NAME OF THE MEDICINAL PRODUCT

Osteofos D3 1200mg/800 I.U. powder for oral suspension

### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet contains:

Colecalciferol (vitamin D3) 20 micrograms (equivalent to 800 I.U.)

Calcium phosphate 3100 mg (equivalent to 1200 mg or 30 mmol of elemental calcium per sachet)

Excipients: also contains Sunset yellow FCF (E110) and sucrose.

For a full list of excipients see section 6.1.

### 3 PHARMACEUTICAL FORM

Powder for oral suspension

*Product imported from Italy:*

White or slightly orange, granular powder.

### 4 CLINICAL PARTICULARS

#### 4.1 Therapeutic Indications

Correction of calcium and Vitamin D deficiency in the elderly.

Osteofos D3 may be used as an adjunct to specific therapy for osteoporosis, in patients with either established vitamin D and calcium combined deficiencies or in those patients at high risk of needing such therapeutic supplements.

#### 4.2 Posology and method of administration

Adults and elderly: 1 sachet/day for oral use

Pour the contents of the sachet into a glass of non-carbonated water. Stir with a spoon to obtain a pleasant-tasting suspension. Drink immediately.

It is advisable to take the preparation during the evening meal.

Children:

The safe or effective use of Osteofos D3 in children has not been established. Therefore, it should not be used in children.

Patients with hepatic dysfunction: No dosage adjustment is required.

Patients with renal dysfunction: Osteofos D3 should not be used in patients with severe renal dysfunction.

### 4.3 Contraindications

Hypersensitivity to active substances or to excipients.

Hypercalcaemia ( $>10.5$  mg/dl), hypercalciuria (300 mg or 7.5 mmol/24 hours), severe renal insufficiency, kidney stones, calcium lithiasis, calcification of tissues, prolonged immobilization accompanied by hypercalciurea and/or hypercalcaemia.

Hypervitaminosis D.

Osteofos D3 is not indicated in children, pregnancy and lactation.

### 4.4 Special warnings and precautions for use

Osteofos D3 must be used with caution in patients with renal insufficiency or when there is an evident tendency for the formation of urinary calculi. Calcaemia and calciuria must be adequately monitored in these patients to prevent the onset of hypercalcaemia. If calciuria levels exceed 7.5 mmol/24 hours (300 mg/24 hours), treatment should be temporary interrupted.

Special caution is also required in the treatment of patients with cardiovascular disease. The effect of cardiac glycosides may be accentuated with the oral administration of calcium combined with Vitamin D. Strict medical supervision, and if necessary, monitoring ECG and calcaemia are necessary.

All other Vitamin D compounds and their derivatives, including food-stuffs which may be fortified with Vitamin D, should be withheld during treatment with Osteofos D3.

The product should be prescribed with caution to patients with sarcoidosis because of possible increased metabolism of Vitamin D to its active form. These patients should be monitored for serum and urinary calcium.

Osteofos D3 contains the colouring agent E110 which can cause allergic-type reactions including asthma. Allergy is more common in those people who are allergic to aspirin.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take Osteofos D3.

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

Absorption of orally administered tetracyclines can be reduced by the simultaneous oral administration of calcium. These two drugs should be taken at least 3 hours apart.

Some diuretics (furosemide, ethacrynic acid), antacids containing aluminium salts and thyroid hormones can inhibit calcium absorption and increase renal and faecal excretion. Thiazide diuretics can reduce urinary excretion of calcium and can induce hypercalcaemia, some antibiotics such as penicillin, neomycin and chloramphenicol can increase its absorption. Monitoring of the serum calcium levels during prolonged treatment is recommended.

Colestyramine, corticosteroids and mineral oils interfere with and reduce Vitamin D absorption, while phenytoin and barbiturates favour its inactivation.

The calcium/digitalis synergism on the heart may cause severe disorders of cardiac function (see section 4.4).

In case of concomitant treatment with bisphosphonate or with sodium fluoride, it is advisable to allow a minimum period of two hours before taking Osteofos D3 (risk of reduction of the gastrointestinal absorption of bisphosphonate and sodium fluoride).

Possible interactions may occur with food (e.g. foods containing phosphate, oxalic or phytinic acid) with a reduction of calcium absorption.

## 4.6 Fertility, pregnancy and lactation

Due to its high vitamin D content, Osteofos D3 is not indicated for use during pregnancy and lactation as the daily dose of Vitamin D should not exceed 600 I.U. Animal studies have shown that vitamin D overdose during pregnancy leads to teratogenic effects and there are no studies on this medicinal product in human pregnancy and lactation. Vitamin D and its metabolites pass into breast milk.

Therefore, Osteofos D3 should not be used during pregnancy and breast-feeding.

## 4.7 Effects on ability to drive and use machines

None.

## 4.8 Undesirable effects

Undesirable effects are listed according to the MedRA System Organ Class.

Since the following reactions have been reported in the post-marketing experience with Osteofos D3, their frequency is not known (cannot be estimated from the available data).

Immune system disorders

Anaphylactic reaction, allergic dermatitis

Metabolism and nutrition disorders

Hypercalcaemia, hypercalciuria

Gastrointestinal Disorders

Nausea, constipation, diarrhoea, epigastric pain

Skin and subcutaneous tissue disorders

Urticaria

## 4.9 Overdose

Overdose can lead to hypervitaminosis D and hypercalcaemia. 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 calcium and vitamin D must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A and cardiac glycosides must be also discontinued. Fluid deficiency should be balanced and individual rescue measures should be decided by the doctor. Rehydration, and, according to the severity, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids. Serum electrolytes, renal function and diuresis must be monitored. In severe cases, ECG (electrocardiogram) and CVP (central venous pressure) should be followed.

The threshold for vitamin D intoxication is between 40,000 and 100,000 IU/day for 1-2 months in persons with normal parathyroid function, for calcium in excess of 2,000 mg per day. Symptoms of vitamin D intoxication are due to hypercalcaemia and should be treated as indicated above.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Calcium, combinations with other drugs.

ATC code: A12AX

Osteofos D3 is a preparation for oral use, in which calcium phosphate is associated with colecalciferol (Vitamin D3).

Calcium and Vitamin D have a fundamental effect on “bone rebuilding” processes and it is for this reason that they are used in those conditions of the elderly patient characterised by a negative calcium balance with low levels of circulating Vitamin D and elevated serum levels of parathormone. This secondary hyperparathyroidism is effectively corrected by the combined effect of tribasic calcium phosphate and Vitamin D3, the active ingredients in Osteofos D3.

Vitamin D3 regulates calcium and phosphate metabolism, guaranteeing calcium absorption by the intestinal mucosa.

### 5.2 Pharmacokinetic properties

Approximately 30% of administered calcium is absorbed in the proximal part of the small intestine. Vitamin D is also quickly absorbed in the intestines after oral administration. The role of bile salts in facilitating absorption is well known. Approximately 40% of plasma calcium is bound to proteins, especially albumin, approximately 1/10 is diffusable, but bound to anions (phosphates); the remaining fraction is diffusable ionic calcium which has a physiological effect.

Vitamin D has a half-life of 19 to 25 hours, and circulates in the plasma bound to a specific protein, an alpha-globulin, and it is accumulated in the body for long periods. In the liver Vitamin D is converted into the derivative 25-hydroxylate (calcidiol) which is put back into the circulation where it binds with a specific alpha-globulin and undergoes further hydroxylation in the kidneys into 1-25 hydroxyderivative (calciterol). Vitamin D is excreted mainly in the bile. Only a small portion of the administered dose is found in the urine.

Calcium is secreted into the gastro-intestinal tract via the saliva, bile and pancreatic secretion. Calcium from these sources, along with the calcium that is not absorbed comprises the portion excreted in the faeces. Of the portion of calcium excreted via the renal system, approximately 2/3 of the filtered calcium is reabsorbed.

Parathormone stimulates calcium reabsorption in the convoluted distal tubules, while Vitamin D increments proximal reabsorption. Part of the calcium is also excreted in perspiration.

### 5.3 Preclinical safety data

Chronic safety evaluation studies in animals show that Vitamin D and calcium combination is generally well tolerated.

Preclinical data reveal no specific hazard for humans, except for toxicity to reproduction (see section 4.6).

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Propylene Glycol  
Sunset Yellow (E110)  
Lemon Cream Flavouring  
Saccharin Sodium  
Anhydrous Citric Acid  
Microcrystalline Cellulose And Carmellose Sodium  
Monopalmitate Sucrose  
Silica Dioxide  
Mannitol

### **6.2 Incompatibilities**

Not applicable.

### **6.3 Shelf Life**

The shelf life expiry date of this product shall be the date shown on the sachets and outer package of the product as marketed in the country of origin.

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

Do not store above 25°C.

### **6.5 Nature and contents of container**

Over-labelled outer carton containing sealed sachets.  
Pack size 30.

### **6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product**

No special requirements

The appearance of the reconstituted product is a smooth orange opaque suspension with visible white granules.

## **7 PARALLEL PRODUCT AUTHORISATION HOLDER**

Imbat Limited  
Unit L2, North Ring Business Park  
Santry  
Dublin 9

## **8 PARALLEL PRODUCT AUTHORISATION NUMBER**

PPA1151/147/1

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 25th February 2011

**10 DATE OF REVISION OF THE TEXT**