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 with known effect: also contains 2 mg Sunset yellow FCF (E110), not more than 8.8 mg sucrose and 640 mg propylene glycol (E 1520) per dose
For the full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Powder for oral suspension
White or slightly orange, granular powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Correction of calcium and Vitamin D deficiency.
OSTEOFOS D3 is indicated in adults and 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

Posology
Adults and elderly
1 sachet/day for oral use.
Patients with hepatic impairment
No dosage adjustment is required.
Patients with renal impairment
OSTEOFOS D3 should not be used in patients with severe renal dysfunction.
Paediatric population
The safety and efficacy of OSTEOFOS D3 in children has not been established; therefore, OSTEOFOS D3 should not be used in this population.
No data are available.
Method of administration
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.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
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 immobilisation 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 temporarily 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.
This medicine 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.
This medicine contains sucrose: patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicines.
This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially 'sodium-free'.
This medicine contains 640 mg propylene glycol (E 1520) in each dosage unit which is equivalent to 9.14 mg / 1 kg.

4.5 Interaction with other medicinal products and other forms of interactions

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

4.6 Fertility, pregnancy and lactation

Pregnancy
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 (see section 4.3).
There are no or limited amount of data from the use of OSTEOFOS D3 in pregnant women. Studies in animals have shown that vitamin D overdose during pregnancy leads to teratogenic effects.
Breast-feeding
Vitamin D / metabolites are excreted in human milk. OSTEOFOS D3 should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

OSTEOFOS D3 has no or negligible influence on the ability to drive and use machines.

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

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

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, polidipsia, 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

Pharmacotherapeutic group: 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

Absorption
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.
Distribution
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.
Biotransformation
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 (calcitriol).
Elimination
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.
Non clinical 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 (E 1520)
Sunset yellow FCF (E110)
Lemon flavouring (containing: natural flavourings, maltodextrin, gum arabic)
Saccharin sodium

Anhydrous citric acid
Microcrystalline cellulose and carmellose sodium
Monopalmitate sucrose
Silica colloidal anhydrous
Mannitol
α-tocopherol
Edible fats
Gelatin
Sucrose
Maize starch.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.
Shelf life after reconstitution: use immediately.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Single, paper-aluminium-polythene bonded, sealed sachets.
The sachets are packaged in cardboard boxes containing 2, 30 or 60 sachets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.
The appearance of the reconstituted product is a smooth orange opaque suspension with visible white granules.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Menarini International Operations Luxembourg S.A.
1, Avenue de la Gare
1611 Luxembourg
Luxembourg

8 MARKETING AUTHORISATION NUMBER

PA0865/007/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28 June 2002

Date of last renewal: 23 September 2009

10 DATE OF REVISION OF THE TEXT

April 2021