Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Cadelius 600mg/1000 IU ordispersible tablet

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One orodispersible tablet contains:
Calcium carbonate 1500 mg (equivalent to 600 mg calcium)
Cholecalciferol (Vitamin D_3) 1000 I.U. (equivalent to 0,025 mg)

Excipients with known effect: aspartame (E 951), lactose, partially hydrogenatedsoya bean oil, sucrose.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Orodispersible tablet

Round flat orodispersible tablets, white to almost white.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Prevention and treatment of calcium and vitamin D deficiency in the elderly. Vitamin D and calcium supplement in addition to specific osteoporosis treatment of patients who are at risk of vitamin D or calcium deficiency, when a dietary supplement as large 600 mg/day of calcium and 1000 IU/day of Vitamin D3 is supposed to be adequate.

4.2 Posology and method of administration

Posology:
Adults and elderly
One orodispersible tablet per day.

Dosage in hepatic impairment
No dose adjustment is required

Dosage in renal impairment
Cadelius should not be used in patients with severe renal impairment (see section 4.3).

Paediatric population:
There is no relevant indication for use of Cadelius orodispersible tablets in children or adolescents

Method of administration:
The tablets may be sucked, they should not be swallowed whole.
The tablets should be taken preferably after meals

The amount of calcium inCadelius is less than the usually recommended daily intake.
Cadelius is therefore primarily to be used by patients with need of D-vitamin substitution but with a dietary intake of calcium of 500 mg-1000 mg per day. The patients dietary intake of calcium should be estimated by the prescriber.

4.3 Contraindications

- Hypersensitivity to calcium, cholecalciferol or to any of the excipients listed in section 6.1.
- Diseases and/or conditions resulting in hypercalcaemia or hypercalciuria.
- Nephrolithiasis.
- Nephrocalcinosis
- Hypervitaminosis D.
- Severe renal impairment or renal failure.

Cadelius contains partially hydrogenated soya-bean oil and must not be used by persons allergic to peanuts or soya.

4.4 Special warnings and precautions for use

Cadelius orodispersible tablets 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.

During long-term treatment, serum 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.

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 metabolised normally and other forms of vitamin D should be used (see section 4.3, contraindications) (see section 4.8).

Cadelius orodispersible tablets should be used cautiously in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

The content of vitamin D (1000 IU) in Cadelius orodispersible tablets should be considered when prescribing other medicinal products containing vitamin D or food supplemented with vitamin D.
Additional doses of calcium or vitamin D should be taken under close medical supervision. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.

Co-administration with tetracyclines or quinolones is usually not recommended, or must be done with precaution.

Cadelius orodispersible tablets are not intended for use in adolescents and children.

The product contains aspartame, source of phenylalanine. May be harmful for people with phenylketonuria. Neither non-clinical nor clinical data are available to assess aspartame use in infants below 12 weeks of age.
The product contains soya bean oil, partially hydrogenated and is contraindicated for patients hypersensitive to peanut or soya (see section 4.3).
The product contains lactose, therefore patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
The product contains sucrose, therefore patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. May be harmful to the teeth.

4.5 Interaction with other medicinal products and other forms of interactions

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

Concomitant use of phenytoin or barbiturates may reduce the effect of vitamin D_3 since the metabolism increases.

Systemic corticosteroids reduce calcium absorption. During concomitant use, it may be necessary to increase the dose of Cadelius.

Hypercalcaemia may increase the toxicity of cardiac glycosides during treatment with calcium and vitamin D. Patients should be monitored with regard to electrocardiogram (ECG) and serum calcium levels.

The efficacy of levothyroxine can be reduced by the concurrent use of calcium, due to decreased levothyroxine absorption. Administration of calcium and levothyroxine should be separated by at least four hours.

If a bisphosphonate is used concomitantly, this preparation should be administered at least one hour before the intake of Cadelius since gastrointestinal absorption may be reduced.

Calcium salts may decrease the absorption of iron, zinc or strontium ranelate. Consequently, the iron, zinc or strontium ranelate preparation should be taken at a distance of two hours from the calcium preparation.
Calcium may also reduce absorption of sodium fluoride, and such preparation should be administered at least three hours before the intake of Cadelius.

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

Calcium carbonate may interfere with the absorption of concomitantly administered tetracycline preparations. For this reason, tetracycline preparations should be administered at least two hours before or four to six hours after oral intake of calcium.

The absorption of quinolone antibiotics may be impaired if administered concomitantly with calcium. Quinolone antibiotics should be taken two hours before or six hours after intake of calcium.

Oxalic acid (found in spinach and rhubarb) and phytic acid (found in whole cereals) may inhibit calcium absorption through formation of insoluble compounds with calcium ions. The patient should not take calcium products within two hours of eating foods high in oxalic acid and phytic acid.

4.6 Fertility, pregnancy and lactation

Pregnancy
Studies in animals have shown reproductive toxicity of high doses of vitamin D (see 5.3). In pregnant women, overdoses of calcium and vitamin D should be avoided as permanent hypercalcaemia has been related to adverse effects on the developing foetus. During pregnancy the daily intake should not exceed 1500 mg calcium and 600 IU vitamin D.
Cadelius should not be used during pregnancy.

Breast-feeding
Cadelius can be used during breast-feeding. Calcium and vitamin D_3 pass into breast milk. This should be considered when giving additional vitamin D to the child.

Fertility
Calcium and vitamin D have no noxious effects on fertility at the recommended dosages (see section 5.3).

4.7 Effects on ability to drive and use machines

There are no data about the effect of this product on driving capacity. An effect is, however, unlikely.

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 (cannot be estimated from the available data): Hypersensitivity reactions such as angioedema or laryngeal edema.

Metabolism and nutrition disorders
Uncommon: Hypercalcaemia and hypercalciuria.

Gastrointestinal disorders
Rare: Constipation, flatulence, nausea, abdominal pain, and diarrhoea.

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

Other special population
Patients with renal impairment: potential risk of hyperphosphatemia, nephrolithiasis and nephrocalcinosis. See section 4.4.

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 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, vitamin D and cardiac glycosides must also be discontinued. Rehydration, and, according to 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 and CVP should be followed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: calcium, combination with other drugs
ATC-code: A12AX

Vitamin D increases the intestinal absorption of calcium.

Administration of calcium and vitamin D_3 counteracts the increase of parathyroid hormone (PTH) which is caused by calcium deficiency and which cause increased bone resorption.

5.2 Pharmacokinetic properties

Absorption: The amount of calcium absorbed through the gastrointestinal tract is approximately 30% of the swallowed dose.
Distribution and metabolism: 99% of the calcium in the body is concentrated in the hard structure of bones and teeth. The remaining 1% is present in the intra- and extracellular fluids. About 50% of the total blood-calcium content is in the physiologically active ionised form with approximately 10% being complexed to citrate, phosphate or other anions, the remaining 40% being bound to proteins, principally albumin. The bioavailability of calcium can be slightly increased by concomitant intake of food.
Elimination: Calcium is eliminated through faeces, urine and sweat. Renal excretion depends on glomerular filtration and calcium tubular reabsorption.

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

Distribution and metabolism: Cholecalciferol and its metabolites circulate in the blood bound to a specific globulin. Cholecalciferol is converted in the liver by hydroxylation to the active form 25-hydroxycholecalciferol. It is then further converted in the kidneys to 1,25- dihydroxycholecalciferol. 1,25-dihydroxycholecalciferol is the metabolite responsible for increasing calcium absorption. Vitamin D which is not metabolised is stored in adipose and muscle tissues.
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 treated with Vitamin D (up to 15 and 12 times the usual daily intake).
High dosages of vitamin D could interfere with endocrinological homeostasis in animals with effects on reproductive function. The extensive use in human allows to exclude potential risks on reproduction, when vitamin D and calcium are assumed at the recommended dosages.
There is further no 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

Maltodextrin
Aspartame (E 951)
Hydroxypropyl cellulose, low-substituted (E463)
Lactose monohydrate
Citric acid, anhydrous (E330)
Orange flavour (natural flavouring substances, maltodextrin, dextrin)
Stearic acid
DL-α-tocopherol (E 307)
Partially hydrogenated soya-bean oil
Gelatin
Sucrose
Maize starch

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years
Cadelius should be used within 60 days after the container is opened.

6.4 Special precautions for storage

Store in the original container, in order to protect from light. Keep container tightly closed in order to protect from moisture.

6.5 Nature and contents of container

High density polyethylene tablet container closed with a PE cap containing a silica gel tab as desiccant.
The tabletcontainercontains 30 or 60 orodispersible tablets
Multipacks contain 60 (2 packs of 30) orodispersible tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.
Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Italfarmaco S.A.
C/ San Rafael 3
Pol. Ind. Alcobendas
Madrid
28108
Spain

8 MARKETING AUTHORISATION NUMBER

PA2102/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 13th April 2017
Date of last renewal: 22nd October 2017

10 DATE OF REVISION OF THE TEXT

April 2022