SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Accrete D3 film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 600 mg calcium (as calcium carbonate 1500 mg) and 10 micrograms of colecalciferol (equivalent to 400 IU vitamin D_3)

Excipients with known effect:

Each film-coated tablet contains 0.3 mg hydrogenated soya-bean oil and 1.52 mg sucrose.

For the full list of excipients, see 6.1

3 PHARMACEUTICAL FORM

Film-coated tablet.
Ochre oval film-coated tablets, scored on one side. When broken the exposed surface is white.
The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Prevention and treatment of vitamin D and calcium deficiency in the elderly.

Vitamin D and calcium supplement as an adjunct to specific osteoporosis treatments of patients who are at risk of vitamin D and calcium deficiency.

4.2 Posology and method of administration

Posology

Adults and elderly

One tablet twice a day (e.g. one tablet in the morning and one tablet in the evening). Dose reduction should be considered as necessary following the monitoring of calcium levels as indicated in section 4.4 and 4.5.

Hepatic impairment

No dose adjustment is required.

Renal impairment

Accrete D3 film-coated tablets should not be used in patients with severe renal impairment.

Children and adolescents

Accrete D3 film coated tablets are not intended for use in children and adolescents.

Method of administration

It is recommended that the film-coated tablet is taken within one and a half hours of a meal with a glass of water or juice, without chewing it. The tablet can be broken in half, if needed.

4.3 Contraindications

- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria (e.g. myeloma, bone metastases or other malignant bone disease, sarcoidosis; primary hyperparathyroidism).
- Nephrolithiasis / nephrocalcinosis
- Severe renal impairment and renal failure
- Hypervitaminosis D
- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1 (including soya or peanut).
- Relative contra-indications are osteoporosis due to prolonged immobilisation, renal stones, severe hypercalciuria.

4.4 Special warnings and precautions for use

Patients who are already taking thiazide diuretics and/or cardiac glycosides should be referred to their doctor prior to concomitant use (i.e. not suitable for pharmacy supply). Concomitant use should be prescribed with caution due to increased risk of hypercalcaemia (see section 4.5)

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 hypercalcaemia or signs of impaired renal function the dose should be reduced or the treatment discontinued. It is advisable to reduce or interrupt treatment temporarily if urinary calcium exceeds 7.5 mmol/24 h (300 mg/24 h).

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 colecalciferol is not metabolised normally and other forms of vitamin D should be used (see section 4.3).

Accrete D3 film-coated tablets should be prescribed with caution to patients suffering from sarcoidosis, due to the 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.

Accrete D3 film-coated tablets should be used with caution in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

The content of vitamin D (400 IU) in Accrete D3 film-coated tablets should be considered when prescribing other medicinal products containing 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. Milk-alkali syndrome (Burnett’s syndrome), i.e. hypercalcaemia, alkalosis and renal impairment can develop when large amounts of calcium are ingested with absorbable alkali.

Accrete D3 film-coated tablets contain sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Allowances should be made for calcium and vitamin D supplements from other sources.

4.5 Interaction with other medicinal products and other forms of interaction

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.

Systemic corticosteroids reduce calcium absorption. During concomitant use, it may be necessary to increase the dose of Accrete D3 film-coated tablets.

Simultaneous treatment with 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.

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.

If a bisphosphonate or sodium fluoride is used concomitantly with Accrete D3 film-coated tablets, these medicinal products should be administered at least three hours before the intake of Accrete D3 film-coated tablet since gastrointestinal absorption may be reduced.

Rifampicin, phenytoin or barbiturates may reduce the activity of vitamin D3, since they increase the rate of its metabolism.

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.

Calcium salts may decrease the absorption of iron, zinc or strontium. Consequently, the iron, zinc or strontium preparation should be taken at a distance of two hours from the calcium preparation.

Calcium salts may reduce the absorption of the estramustin or thyroid hormones. It is recommended that taking Accrete D3 film-coated tablets be spaced at least 2 hours from these medicines.

Oxalic acid (found in spinach, sorrel and rhubarb), phosphate 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

Accrete D3 film-coated tablets may be given during pregnancy in cases of calcium and vitamin D3 deficiency.

During pregnancy the daily dose should not exceed 1500 mg of calcium and 600 IU of vitamin D. Animal studies have shown toxic effects on reproduction at high doses of vitamin D. In pregnant women, all calcium or vitamin D overdoses must be avoided as prolonged hypercalcaemia in pregnancy may lead to retardation of physical and mental development, supravalvular aortic stenosis and retinopathy in the child. There are no indications that Vitamin D_3 at therapeutic doses is teratogenic in human.

Breast-feeding

Accrete D3 film-coated tablets can be used during breast-feeding. Calcium and vitamin D pass into breast milk. This should be considered when giving additional vitamin D to the child.

Fertility

There is no known harmful effect of endogenous levels of calcium and vitamin D in the normal range on fertility. There are no data available on the effect of Accrete D3 film-coated tablets on fertility.

4.7 Effects on ability to drive and use machines

There are no data on the effect of this product on the ability to driver or use machines, however an effect is unlikely.

4.8 Undesirable effects

Adverse reactions are listed below, by system organ class and frequency. Frequencies are defined as:

uncommon (>1/1,000 to <1/100); rare (>1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

Immune system disorders

Not known: Hypersensitivity reactions including pruritus, wheezing, urticaria and oropharyngeal swelling have been reported in the post-marketing environment.

Metabolism and nutrition disorders

Uncommon: Hypercalcaemia and hypercalciuria.

Very rare: Seen usually only in overdose, see 4.9: Milk-alkali syndrome

Gastrointestinal disorders

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

Very rare: Dyspepsia

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 the Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard.

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.

Milk-alkali syndrome may occur in patients who ingest large amounts of calcium and absorbable alkali. Symptoms are frequent urge to urinate, continuing headache, continuing loss of appetite, nausea or vomiting, unusual tiredness or weakness, hypercalcaemia, alkalosis and renal impairment.

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. Emptying of the stomach in patients with impaired consciousness. 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 vitamin D and/or other drugs

ATC code: A12AX

Vitamin D increases the intestinal absorption of calcium.

Administration of calcium and vitamin D_3 (colecalciferol) counteracts the increase of parathyreoid hormone (PTH), which is caused by calcium deficiency and which causes increased bone resorption.

A clinical study of institutionalised patients suffering from vitamin D deficiency indicated that a daily intake of two tablets of calcium 500 mg/Vitamin D 400 IU for six months normalised the value of the 25-hydroxylated metabolite of Vitamin D_3 and reduced secondary hyperparathyroidism and alkaline phosphatases.

An 18-month double blind, placebo controlled study including 3270 institutionalised women aged 84±6 years that received supplementation of vitamin D (800 IU/day) and calcium phosphate (corresponding to 1200 mg/day of elemental calcium), showed a significant decrease of PTH secretion. After 18 month, an “intent-to treat” analysis showed 80 hip fractures in the calcium-vitamin D group and 110 hip fractures in the placebo group ($p=0.004$). A follow-up study after 36 months showed 137 women with at least one hip fracture in the calcium-vitamin D group ($n=1176$) and 178 in the placebo group ($n=1127$, $p<0.02$).

5.2 Pharmacokinetic properties

Calcium

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.

Elimination: Calcium is eliminated through faeces, urine and sweat. Renal excretion depends on glomerular filtration and calcium tubular reabsorption.

Vitamin D

Absorption: Vitamin D3 is absorbed in the small intestine.

Distribution and metabolism: Colecalciferol and its metabolites circulate in the blood bound to a specific globulin. Colecalciferol is converted in the liver by hydroxylation to the active form 25-hydroxycolecalciferol. It is then further converted in the kidneys to 1,25 hydroxycolecalciferol. 1,25 hydroxycolecalciferol 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. 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

Tablet core:

Magnesium stearate

Crospovidone (Type A)

Copovidone (K-value: 25.2-30.8)

Microcrystalline cellulose

Sucrose

Gelatin

all-rac -α-Tocopherol (E307)

Hydrogenated soya-bean oil

Maize starch

Coating (Sepifilm 4202 yellow):

Yellow iron oxide (E172)

Hypromellose (15 mPa s)

Titanium dioxide (E171)

Macrogol 3350

Talc

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

10 film-coated tablets are packed in transparent, colourless PVC/Al blister

3 or 6 blisters are in a box.

Pack size: 30, 60 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Thornton & Ross Ltd., Linthwaite, Huddersfield, HD7 5QH, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 00240/0498

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

14/08/2014

10 DATE OF REVISION OF THE TEXT

23/11/2023