SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Adcal-D_3 Dissolve 1500mg/400IU Effervescent Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

One effervescent tablet contains:
1500 mg calcium carbonate (equivalent to 600 mg or 15 mmol elemental calcium) 400 I.U. or 10 micrograms colecalciferol (vitamin D_3) as colecalciferol concentrate 'powder form'

This product also contains sucrose (part of the vitamin D_3 concentrate: approximately 0.77 milligrams per tablet), sodium (approximately 42.03 mg per tablet) and sorbitol (approximately 0.6 milligrams per tablet). Please refer to Section 4.4 for further details.

For a full list of excipients see Section 6.1

3 PHARMACEUTICAL FORM

White, round, lemon flavoured effervescent tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

As an adjunct to specific therapy for osteoporosis and in situations requiring therapeutic supplementation of malnutrition e.g. in pregnancy and established vitamin D dependent osteomalacia.

The prevention and treatment of calcium deficiency/vitamin D deficiency especially in the housebound and institutionalised elderly subjects. Deficiency of the active moieties is indicated by raised levels of PTH, lowered 25-hydroxy vitamin D and raised alkaline phosphatase levels which are associated with increased bone loss.

4.2 Posology and method of administration

Oral.

Adults and elderly and children over 12 years of age:	Take 2 effervescent tablets daily, preferably one tablet each morning and evening. The effervescent tablets should be dissolved in a glass of water (approx. 200ml) and drunk immediately
Children:	Not recommended for children under 12 years.

4.3 Contraindications

Absolute contra-indications are hypercalcaemia resulting for example from myeloma, bone metastases or other malignant bone disease, sarcoidosis; primary hyperparathyroidism and vitamin D overdosage. Severe renal failure. Hypersensitivity to any of the tablet excipients.

Relative contra-indications are osteoporosis due to prolonged immobilisation, renal stones, severe hypercalciuria.

4.4 Special warnings and precautions for use

Patients with mild to moderate renal failure or mild hypercalciuria should be supervised carefully including periodic checks of plasma calcium levels and urinary calcium excretion.

In patients with a history of renal stones urinary calcium excretion should be measured to exclude hypercalciuria.

With long-term treatment it is advisable to monitor serum and urinary calcium levels and kidney function, and reduce or stop treatment temporarily if urinary calcium exceeds 7.5mmol/24 hours (300mg/24 hours).

During concomitant treatment with other high-dose sources of vitamin D and/or medications affecting serum calcium levels or absorption, or nutrients containing calcium (see section 4.5), there is a risk of hypercalcaemia and milk-alkali syndrome (See section 4.9). In these patients, serum calcium levels and renal function should be monitored.

Caution is required in patients receiving treatment for cardiovascular disease (see Section 4.5 – thiazide diuretics and cardiac glycosides including digitalis).

Adcal-D_3 Dissolve should also be used with caution in other patients with increased risk of hypercalcaemia e.g. patients with sarcoidosis or those suffering from malignancies.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insuffiency should not take this medicine.

Each tablet contains a small amount of sugar (about 0.77 mg per tablet) and may be harmful to teeth if used for a prolonged period.

This medicinal product contains approximately 42.03 mg sodium per tablet, equivalent to 2.1% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

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

The risk of hypercalcaemia should be considered in patients taking thiazide diuretics since these drugs can reduce urinary calcium excretion. Hypercalcaemia must be avoided in digitalised patients.

Certain foods (e.g. those containing oxalic acid, phosphate or phytic acid) may reduce the absorption of calcium.

Concomitant treatment with phenytoin or barbiturates can decrease the effect of vitamin D because of metabolic activation. Concomitant use of glucocorticoids can decrease the effect of vitamin D.

The effects of digitalis and other cardiac glycosides may be accentuated with the oral administration of calcium combined with Vitamin D. Strict medical supervision is needed and, if necessary, monitoring of ECG and calcium.

Calcium salts may reduce the absorption of thyroxine, bisphosphonates, sodium fluoride, quinolone or tetracycline antibiotics, zinc, strontium ranelate and iron. It is advisable to allow a minimum period of four hours before taking calcium.

Concomitant treatment with orlistat may reduce absorption of vitamin D.

4.6 Fertility, Pregnancy and lactation

During pregnancy and lactation treatment with Adcal-D_3 Dissolve should always be under the direction of a physician. During pregnancy and lactation, requirements for calcium and vitamin D are increased but in deciding on the required supplementation allowances should be made for availability of these agents from other sources. If Adcal-D_3 Dissolve and iron supplements are both required to be administered to the patient, they should be taken at different times (see Section 4.5).

Overdoses of vitamin D have shown teratogenic effects in pregnant animals. However, there have been no studies on the use of this medicinal product in human pregnancy and lactation. In humans, long term hypercalcaemia can lead to physical and mental retardation, aortic stenosis and retinopathy in a new born child. Vitamin D and its metabolites pass into the breast milk.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Hypersensitivity reactions including pruritus, wheezing, urticaria, oropharyngeal swelling and angioedema have been reported in the post-marketing environment.

The use of calcium supplements has, rarely, given rise to mild gastro-intestinal disturbances, such as constipation, flatulence, nausea, gastric pain or diarrhoea. Following administration of vitamin D supplements occasional skin rash has been reported. Hypercalciuria, and in rare cases hypercalcaemia, have been seen with long term treatment at high dosages.

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

The most serious consequence of acute or chronic overdose is hypercalcaemia due to vitamin D toxicity. Symptoms may include nausea, vomiting, polyuria, anorexia, weakness, apathy, thirst and constipation. Chronic overdoses can lead to vascular and organ calcification as a result of hypercalcaemia. Treatment should consist of stopping all intake of calcium and vitamin D and rehydration.

Milk-alkali syndrome may occur in patients who ingest large amounts of calcium.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Calcium, combinations with vitamin D and/or other drugs, ATC code: A12AX

Strong evidence that supplemental calcium and vitamin D_3 can reduce the incidence of hip and other non-vertebral fractures derives from an 18 month randomised placebo controlled study in 3270 healthy elderly women living in nursing homes or apartments for elderly people. A positive effect on bone mineral density was also observed.

In patients treated with 1200mg elemental calcium and 800IU vitamin D_3 daily, i.e. the same dose delivered by two tablets of Adcal-D_3 Dissolve, the number of hip fractures was 43% lower (p=0.043) and the total number of non vertebral fractures was 32% lower than among those who received placebo. Proximal femur bone mineral density after 18 months of treatment increased 2.7% in the calcium/vitamin D_3 group and decreased 4.6% in the placebo group ($p < 0.001$). In the calcium/vitamin D_3 group, the mean serum PTH concentration decreased by 44% from baseline at 18 months and serum 25-hydroxy-vitamin D concentration had increased by 162% over baseline.

Analysis of the intention-to-treat results showed a decreased probability of both hip fractures ($p = 0.004$) and other fractures ($p < 0.001$) in the calcium/vitamin D_3 treatment group. Analysis of the other two populations (active treatment and those treated and followed for 18 months) revealed comparable results to the intention-to-treat analysis. The odds ratio for hip fractures among women in the placebo group compared with those in the calcium/vitamin D_3 group was 1.7 (95% CI 1.0 to 2.8) and that for other nonvertebral fractures was 1.4 (95% CI 1.4 to 2.1). In the placebo group, there was a marked increase in the incidence of hip fractures over time whereas the incidence in the calcium/vitamin D_3 group was stable. Thus treatment reduced the age-related risk of fracture at 18 months ($p = 0.007$ for hip fractures and $p = 0.009$ for all non-vertebral fractures). At 3 years follow-up, the decrease in fracture risk was maintained in the calcium/vitamin D_3 group.

5.2 Pharmacokinetic properties

The pharmacokinetic profiles of calcium and its salts are well known. Calcium carbonate is converted to calcium chloride by gastric acid. Calcium is absorbed to the extent of about 15-25% from the gastro-intestinal tract while the remainder reverts to insoluble calcium carbonate and calcium stearate, and is excreted in the faeces.

The pharmacokinetics of vitamin D is also well known. Vitamin D is well absorbed from the gastro-intestinal tract in the presence of bile. It is hydroxylated in the liver to form 25-hydroxycolecalciferol and then undergoes further hydroxylation in the kidney to form the active metabolite 1, 25 dihydroxycolecalciferol (calcitriol). The metabolites circulate in the blood bound to a specific α-globin. Vitamin D and its metabolites are excreted mainly in the bile and faeces.

5.3 Preclinical safety data

Calcium carbonate and vitamin D are well known and widely used materials and have been used in clinical practice for many years. As such, toxicity is only likely to occur in chronic overdosage where hypercalcaemia could result.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

citric acid anhydrous

malic acid

sodium hydrogen carbonate (E500)

sodium cyclamate (E953)

lemon flavour BSL Code 119 *containing* lemon oil, lime flavouring, sorbitol (E420), mannitol (E421), gluconolactone, maltodextrin and acacia

sodium carbonate (E500)

maltodextrin

saccharin sodium (E954)

modified starch

sucrose

sodium ascorbate

triglycerides, medium chain

silica, colloidal anhydrous

all-rac-alpha-tocopherol

6.2 Incompatibilities

None

6.3 Shelf life

2 Years

6.4 Special precautions for storage

Do not store above 30°C.

Keep the container tightly closed.

6.5 Nature and contents of container

Packs of 4 x 14 effervescent tablets in a carton.

Each unit of 14 effervescent tablets is in an aluminium or polypropylene tube with a polyethylene stopper.

Contains a desiccant.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

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SL6 8BN

United Kingdom

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