Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Bellcalcid Calcium Carbonate 1500 mg and Colecalciferol 400 I.U. Effervescent Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Effervescent tablet
A white, round effervescent tablet, with the odour and flavour of lemon.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Correction of combined vitamin D_3 and calcium deficiencies.
Vitamin D_3 and calcium supplementation as an adjunct to specific treatment for osteoporosis in patients, where combined calcium and vitamin D deficiencies have been diagnosed or at high risk of such deficiencies.

4.2 Posology and method of administration

Adults take 1 - 2 effervescent tablets daily (equivalent to 600-1200 mg of calcium and 400-800 I.U. of vitamin D_3). For pregnancy and lactation, see paragraph 4.6 ‘Pregnancy and Lactation’.

The effervescent tablets should be dissolved in a glass of water (approx. 200ml) and drunk immediately.

Oral use - For adults only.

4.3 Contraindications

Hypersensitivity to one of the constituents of the effervescent tablet
- Hypercalcaemia.
- Hypercalciuria.
- Kidney stones.
- Nephrocalcinosis.
- Primary hyperparathyroidism.
- Vitamin D overdose.
- Myeloma.
- Bone metastases.

Long term immobilisation in combination with hypercalciuria and/or hypercalcaemia.

4.4 Special warnings and precautions for use

During long-term use, serum and urinary calcium levels as well as kidney function should be monitored through the measurement of serum creatinine levels. Dosage should be reduced or treatment temporarily suspended if urinary calcium excretion exceeds 7.5mmol / 24 hours (300 mg / 24 hours).

Monitoring of kidney function is especially important when there is concomitant treatment with digitalis glycosides and thiazide diuretics. Special care is required on concurrent treatment with bisphosphonates, sodium fluoride or tetracycline (see 4.5 Interactions).

The dosage of vitamin D per dosage from (400 I.U.) should be taken into account on concurrent administration of other vitamin D preparations.

Since Bellcalcid already contains vitamin D, additional vitamin D or calcium preparations should only be taken under strict medical supervision. In such cases, it is essential to carry out a weekly check on serum and urinary calcium levels.

In patients suffering from sarcoidosis Bellcalcid should be taken under medical supervision because of the risk of hypercalcaemia due to increased metabolism of vitamin D to its active metabolite. These patients should have the urinary and plasma levels monitored.

Bellcalcid should be used with caution in patients with renal dysfunction and checks on calcium and phosphate homeostasis should be undertaken.

In patients with renal insufficiency, vitamin D in the form of colecalciferol is not metabolised normally and other forms of vitamin D should be used.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine. Hydrogenated soya oil may contain peanut protein and is therefore contraindicated in patients who are allergic to peanut or soya oil.

Information for diabetics
1 effervescent tablet contains 0.01 Bread Units and is therefore suitable for diabetics.

4.5 Interaction with other medicinal products and other forms of interaction

During treatment with digitalis glycosides, oral calcium combined with vitamin D may increase toxicity of the digitalis glycosides (risk of cardiac arrhythmias). Close clinical surveillance, if necessary coupled with ECG and serum calcium monitoring is essential.

When used in combination with bisphosphonates or sodium fluoride, it is recommended that at least two hours elapse before the calcium preparation is taken, as otherwise absorption of the bisphosphonate or sodium fluoride is reduced.

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

Thiazide diuretics lead to a decrease of calcium excretion in urine. Serum calcium levels should therefore be monitored during treatment with thiazide diuretics.

Concomitant administration of rifampicin, phenytoin or barbiturates may accelerate the metabolism and hence reduce the effects of vitamin D_3.

An interval of at least two hours should be observed between ingestion of cholestyramine and Bellcalcid as otherwise the absorption of vitamin D_3 is reduced.

Simultaneous administration of glucocorticoids may reduce the effects of vitamin D_3.

Since calcium can impair the absorption of orally administered tetracycline, it is recommended to take the preparation at least three hours after the tetracycline.
Interaction may occur with some foods (for example, food containing oxalic acid, phosphates or phytinic acid or having a high fibre content).

4.6 Pregnancy and lactation

During pregnancy and lactation, combined vitamin D and calcium deficiencies can be corrected. The daily intake should not exceed 1,500 mg of calcium and 600 I.U. of vitamin D_3. Therefore, the daily dose must not exceed 1 tablet.
Overdoses of vitamin D have been shown to have teratogenic effects in animal experiments.
In pregnant women, overdosages of vitamin D_3 should be avoided, since prolonged hypercalcaemia has been sometimes associated with retardation of physical and mental development, supravalvular aortic stenosis and retinopathy in the child.
There are, however, several case reports of administration of very high vitamin D doses in hypoparathyroidism in the mother, where normal children were born.
Calcium passes slightly into breast-milk, without having a negative effect on children. Vitamin D and its metabolites also pass into breast-milk. This should be considered when giving additional vitamin D to the child.
In pregnant and lactating women, the calcium preparation should be taken at a distance of two hours from a meal due to a possible decrease of iron absorption.

4.7 Effects on ability to drive and use machines

An unfavourable effect of the preparation on ability to drive or operate machines is very unlikely.

4.8 Undesirable effects

Constipation, bloating, nausea, gastric pain, diarrhoea, hypercalciuria, hypercalcaemia.

4.9 Overdose

Overdosage leads to hypercalciuria and hypercalcaemia with the following symptoms:
Nausea, vomiting, thirst, polydipsia, polyuria, dehydration, constipation. Chronic overdosage with resulting hypercalcaemia can cause vascular and organic calcification.

The threshold for vitamin D intoxication is between 40,000 and 100,000 I.U/day for 1-2 months in persons with normal parathyroid function, for calcium in excess of 2,000 mg per day.

Treatment
In the case of an intoxication, treatment should be stopped immediately and the fluid deficiency should be balanced.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:	Minerals	(A12)
	Vitamins	(A11)

Bellcalcid is a fixed combination of calcium and vitamin D. The high calcium and vitamin D concentration in each dose unit enables sufficient absorption of calcium with a limited number of doses. Vitamin D is involved in calcium-phosphorus metabolism. It allows the active absorption of calcium and phosphorus from the intestine and their uptake by bone. Supplementation with calcium and vitamin D_3 corrects latent vitamin D deficiency and secondary hyperparathyroidism.

In a double-blind placebo controlled study of 18 months, including 3270 women aged 84 ± 6 and living in nursing homes, supplemented with colecalciferol (800 IU/day) + Calcium (1.2 g/day), a significant decrease in Parathyroid Hormone (PTH) secretion has been observed. After 18 months, the results of the 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). So in the conditions of this study, the treatment of 1387 women prevented 30 hip fractures.

After 36 months of follow-up, 137 women presented 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 carbonate
Absorption:
On dissolution of the effervescent tablet, the calcium carbonate is converted in the presence of citric acid to soluble calcium citrate. Some 30-40% of the ingested dose of calcium is absorbed, predominantly in the proximal part of the small intestine.

Elimination:
Calcium is excreted in the urine, faeces and in sweat. Urinary excretion depends on glomerular filtration and tubular resorption.

Vitamin D_3:
Absorption:
Vitamin D_3 is absorbed in the intestine and transported by protein binding in the blood to the liver (where it undergoes the first hydroxylation to 25-hydroxycolecalciferol) and to the kidneys (second hydroxylation to 1, 25-di-hydroxycolecalciferol), the actual active metabolite of vitamin D_3.

Non-hydroxylated vitamin D_3 is stored in muscle and adipose tissues.

Elimination:
The plasma half-life is in the order of several days; vitamin D_3 is eliminated in the faeces and urine.

5.3 Preclinical safety data

No other relevant data is available that has not been mentioned elsewhere in the Summary of Product Characteristics (see 4.6 Pregnancy and Lactation; 4.9 Overdose).

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid anhydrous (E330)
Malic acid (E296)
Sodium hydrogen carbonate (E500)
Sodium cyclamate
Lemon flavouring (contains: lemon oil, mannitol (E421), sorbitol (E420), dextrin, D-glucono-1,5-lactone (E575), acacia (E414))
Sodium carbonate anhydrous (E500)
Maltodextrin
Saccharin sodium
Sucrose
Gelatin
Maize starch

Partially hydrogenated soya oil
All-rac-α-tocopherol (E307)

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 30^{o}C.
Keep the container tightly closed.

6.5 Nature and contents of container

Packs of 20, 40, (2 x 20), 60 (3 x 20), and 100 (5 packs of 20) effervescent tablets. Each unit of 20 tablets is in a aluminium or polypropylene tube with polyethylene stopper containing a desiccant.

Not all pack sizes may be marketed.

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.

7 MARKETING AUTHORISATION HOLDER

BellPharma Limited
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8 MARKETING AUTHORISATION NUMBER

PA 1185/3/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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