SELECT THE REQUIRED INFORMATION

PROFESSIONAL INFORMATION

PATIENT INFORMATION LEAFLET

COMPLEMENTARY MEDICINE: HEALTH SUMPLEMENT
This unregistered medicine has not been evaluated by the SAHPRA for its quality, safety or intended use.

SCHEDULING STATUS: S0

1. NAME OF THE MEDICINE

BEROCCA EXPERT Vit D, Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Berocca® Expert Vit D is a triple layer tablet containing vitamin D, vitamin K and calcium.
Each triple layer contains the following active ingredients:

Ingredient Name	Quantity
Vitamin K2 (menaquinone)	44 µg
Vitamin D3 (cholecalciferol)	25 µg
Calcium (calcium carbonate)	500 mg

Sugar free.

For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
Yellow, white and red oblong triple layer tablet.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Berocca® Expert Vit D Tablets contains calcium with sufficient vitamin D. Berocca® Expert Vit D Tablets intake together with a healthy diet and regular exercise, may reduce the risk of developing osteoporosis. Berocca® Expert Vit D Tablets contributes to the development and maintenance of bones and teeth. This product is also a factor in the maintenance of good health.

4.2. Posology and method of administration

Posology

For oral use.
The recommended intake for adults is one tablet a per day. Consume the tablet with sufficient water.

4.3. Contraindications

- Hypersensitivity to any of the active substances or to any of the excipients listed in section 6.1.

- Existing Hypervitaminosis D
- Hypercalcaemia
- Severe hypercalciuria

4.4. Special warnings and precautions for use

Do not exceed the labelled dose. Acute and chronic overdose increases the risk of adverse effects. Allowance should be made for intake of the vitamins and minerals from all other sources including fortified foods, dietary supplements, and concomitant medications (see section 4.9). In particular, vitamin D can be harmful to health.
Individuals receiving other single vitamins or multivitamin preparations, any other medication or those under medical care should consult a health care professional before use of the product (see sections 4.5). In particular, patients receiving vitamin K antagonists and/or any other anticoagulation treatment must consult a health care professional prior to use.
Concomitant treatment with vitamin D analogues should be avoided due to risk of hypervitaminosis D and/or hypercalcaemia. If concomitant use is deemed essential, the serum and urinary levels of calcium must be regularly monitored (see section 4.5).
Since calcium, and vitamin D may have an effect on stone formation, patients with nephrolithiasis or urolithiasis should use caution when using vitamin supplements.
Separate intake of the product from other medications by four (4) hours unless otherwise specified (see section 4.5).

4.5. Interaction with other medicines and other forms of interaction

Manifold potential interactions are reported in the literature for the single ingredients, thus individuals receiving any other medication, dietary/food supplements, or those under medical care should consult a physician or health care professional before use of the product. When used as recommended no specific interactions are expected.
It has been reported that vitamin K containing drugs should be used with caution in patients receiving anticoagulants.
Thus, patients receiving any other medication or those under medical care should consult a physician or health care professional before taking this medicinal product.

Drug interactions

Active Ingredient	Drug	Description
Vitamin K	Warfarin	Very high dietary (>150 µg/day) or supplemental intake of vitamin K may compromise the anticoagulant effect of warfarin. It is recommended to avoid fluctuation in vitamin K intake that might interfere with the adjustment of their anticoagulant dose.
Vitamin D3	Vitamin D analogues (e.g. Calcitriol)	Concomitant treatment with vitamin D analogues should be avoided due to increased risk of hypervitaminosis D and/or hypercalcaemia. Vitamin D analogues include ergocalciferol and calcitriol. If deemed essential, serum and urine calcium levels should be monitored.
	Cholestyramine	Gastro-intestinal absorption of vitamin D is decreased with simultaneous administration. Separate intake of the product and these medications by four hours, unless otherwise specified, will minimize risk for any interaction.

Active Ingredient	Drug	Description
	Thiazide diuretics (e.g. Bendroflumethiazide)	Thiazide diuretics (e.g., Hygroton®, Lozol®, and Microzide®) decrease urinary calcium excretion. The combination of these diuretics with vitamin D supplements (which increase intestinal calcium absorption) might lead to hypercalcemia, especially among older adults and individuals with compromised renal function or hyperparathyroidism.
Calcium	Tetracycline antibiotics	As a polyvalent cation; calcium forms complexes with certain substances resulting in decreased absorption of both substances. Separate intake of the product and these medications by 4 hours, unless otherwise specified, will minimize risk for this interaction.
	Quinolone antibiotics	
	Lithium	
	Levothyroxine	
	Dolutegravir	

Food interaction

Since oxalic acid (found in spinach and rhubarb) and phytic acid (found in fiber-containing whole-grain products) may inhibit calcium absorption, it is not recommended to take this product within two hours of eating foods containing high oxalic acid and phytic acid concentrations.

4.6. Fertility, pregnancy and lactation

Fertility

There is no evidence suggestive that normal endogenous levels of the vitamins and minerals in the product cause adverse reproductive effects in humans.

Pregnancy & Breastfeeding

Berocca® Expert Vit D Tablets is not intended for use during pregnancy and lactation.

4.7. Effects on ability to drive and use machines

The product has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable effects

The listed adverse reactions have been identified during post-approval use of the product. Because these reactions are reported voluntarily, it is not possible to estimate their frequency.

Gastrointestinal disorders

Gastrointestinal and abdominal pain, constipation, diarrhoea, nausea and vomiting may occur.

Immune system disorders

In isolated cases this product may cause allergic or anaphylactic reaction. Symptoms may include hives, facial swelling, wheezing, skin reddening, rash, blisters, and shock. If an allergic reaction occurs, treatment must be stopped, and a health care professional consulted.

Metabolism and nutrition disorders

Hypercalciuria.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. Alternatively, you can report to Bayer SafeTrack site (https://www.safetrack-public.bayer.com) or via the Bayer website (www.bayer.co.za). By reporting side effects, you can help provide more information on the safety of Berocca® Expert Vit D Tablets.

4.9. Overdose

There is no evidence that this product can lead to an overdose when used as recommended.
Most, if not all reports concerning overdoses of vitamins and minerals are associated with concomitant intake of high dosed single and/or multivitamin preparations. Acute or long-term overdose can cause hypervitaminosis D and hypercalcaemia.
Uncharacteristic initial symptoms, such as abrupt onset of headache, confusion, and gastrointestinal disturbances such as constipation, diarrhoea, nausea, and vomiting might be indicative for an acute overdose.
If such symptoms occur, treatment must be stopped and a health care professional consulted.
Specific clinical manifestations may include the following:
Vitamin D
Chronic ingestions of vitamin D in excess of 4 000 IU/day (100 µg/day) can result in toxicity Many of the effects of chronic vitamin D toxicity are due to induced hypercalcaemia. Symptoms may include anorexia, nausea, vomiting, and weight loss.
Maternal hypercalcemia, possibly caused by excessive vitamin D intake during pregnancy, has been associated with hypercalcemia in neonates, which may lead to supravalvular aortic stenosis syndrome, the features of which may include retinopathy, mental or growth retardation, strabismus and other effects.
Calcium
Hypercalcemia (serum levels greater than 10,5 mg/dL [2.63 mmol/L]) and hypercalciuria (urinary calcium levels higher than 250 mg/day in women and 275 mg/day in men) are rare in healthy people and usually result from cancer, primary hyperparathyroidism, and other conditions. Hypercalcemia and hypercalciuria can cause poor muscle tone, renal insufficiency, hypophosphatemia, constipation, nausea, weight loss, fatigue, polyuria, heart arrhythmias, and a higher risk of CVD mortality

If overdose with the product is suspected, intake should be stopped, and a health care professional consulted for treatment of clinical manifestations.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacological classification: category D 34.12 (Multiple substance formulation).
Multivitamins, other combinations constitute a distinct pharmacotherapeutic group under the ATC code A11AA02.

Vitamins and minerals, including trace elements, are essential micronutrients required by every living cells, with key roles in numerous homeostatic processes that enable the body to produce enzymes, hormones and other substances that are essential for energy production, cell maintenance and repair, immune function and recovery from illness, blood formation, and maintenance of vital organs.
Minerals (including trace elements) are inorganic substances and must be taken up through food, whereas vitamins can be synthesized by many species. Humans, however, have lost this ability and cannot synthesize most vitamins in sufficient amounts, and are therefore dependent on a continuous exogenous supply.
Vitamin D promotes calcium absorption in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal bone mineralization and to prevent hypocalcemic tetany (involuntary contraction of muscles, leading to cramps and spasms). It is also needed for bone growth and bone remodelling by osteoblasts and osteoclasts. Without sufficient vitamin D, bones can become thin, brittle, or misshapen. Vitamin D sufficiency prevents rickets in children and osteomalacia in adults. Together with calcium, vitamin D also helps protect older adults from osteoporosis.
Vitamin K functions as a coenzyme for vitamin K-dependent carboxylase, an enzyme required for the synthesis of proteins involved in hemostasis (blood clotting) and bone metabolism and other diverse physiological functions. Prothrombin (clotting factor II) is a vitamin K-dependent protein in plasma that is directly involved in blood clotting.
Calcium participates in numerous physiological processes and enzyme systems and plays essential roles in blood clotting, muscle contraction, nerve transmission, and bone and tooth formation. It interacts in many of these processes in a complex way with magnesium and vitamin B6. Calcium also activates a series of reactions including fatty acid oxidation, the tricarboxylic acid cycle (Krebs cycle) and glucose-stimulated insulin release.

5.2. Pharmacokinetic properties

Vitamin K:
Absorption:
Like dietary lipids and other fat-soluble vitamins, ingested vitamin K is incorporated into mixed micelles via the action of bile and pancreatic enzymes, and it is absorbed by enterocytes of the small intestine. From there, vitamin K is incorporated into chylomicrons, secreted into the lymphatic capillaries, transported to the liver, and repackaged into very low-density lipoproteins.
Distribution
Vitamin K is present in the liver and other body tissues, including the brain, heart, pancreas, and bone.
Metabolism & Excretion:
Vitamin K is rapidly metabolized and excreted. Based on phylloquinone measurements, the body retains only about 30% to 40% of an oral physiological dose, while about 20% is excreted in the urine and 40% to 50% in the faeces via bile. This rapid metabolism accounts for vitamin K's relatively low blood levels and tissue stores compared to those of the other fat-soluble vitamins.
Vitamin D:
Absorption:
In foods and dietary supplements, vitamin D has two main forms, D_2 (ergocalciferol) and D_3 (cholecalciferol), that differ chemically only in their side-chain structures. Both forms are well absorbed in the small intestine. Absorption occurs by simple passive diffusion and by a mechanism that involves intestinal membrane carrier proteins. The concurrent presence of fat in the gut enhances vitamin D absorption, but some vitamin D is absorbed even without dietary fat. Neither aging nor obesity alters vitamin D absorption from the gut
Distribution:

Once absorbed, Vitamin D is transported in the bloodstream bound to Vitamin D-binding protein (DBP) and lipoproteins. It is distributed to various tissues, including the liver, adipose tissue, and muscle, where it can be stored for later use.
Metabolism:
Vitamin D undergoes two hydroxylation steps for activation. The first hydroxylation occurs in the liver, converting Vitamin D to 25-hydroxyvitamin D (calcidiol). The second hydroxylation occurs primarily in the kidneys, forming the physiologically active 1,25-dihydroxyvitamin D (calcitriol). This active form of Vitamin D is crucial for calcium and phosphate homeostasis, bone health, and modulation of immune function.
Excretion:
Excretion of Vitamin D and its metabolites is primarily through bile and feces. The metabolites are excreted slowly due to their fat-soluble nature, which allows for prolonged retention in the body. Renal excretion plays a minor role in the elimination of Vitamin D metabolites.

Calcium:
Absorption:
The amount of calcium absorbed depends on its interaction with other dietary constituents, and on physiological factors such as calcium-regulating hormones and stage of the life span. In general, the absorption of calcium supplements is better if they are taken with a meal. This may be because the meal stimulates gastric secretion and delays emptying, so that the calcium sources are better dispersed and dissolved. There are two routes of calcium absorption in the intestine. One is an active, saturable, transcellular process that occurs mainly in the duodenum and proximal jejunum and is regulated by vitamin D. Ileal absorption may also be affected by vitamin D status. The other pathway of calcium absorption is a passive, nonsaturable, paracellular route that is independent of vitamin D regulation and occurs throughout the small intestine. The amount of calcium absorbed by this way depends primarily on its quantity and availability in the diet. Intakes above as little as 3 mmol (120 mg) in a meal will probably be absorbed passively by the small intestine. Most calcium absorption occurs in the ileum, where food remains for the longest time.
Distribution:
Because more than 99 % of the body's calcium is in bone, the skeleton is the major storage site for the maintenance of extracellular fluid (ECF) calcium. In the short term, negative calcium balance involves a harmless mobilization of bone calcium. In the longer term, the chronic removal of skeletal calcium has adverse effects on bone strength. The level of ionized calcium in plasma is controlled by an integrated response of the calcium-regulating hormones that affect calcium transport in the intestine, bone and kidney. Of these the most important are parathyroid hormone (PTH), calcitonin and vitamin D. Serum calcium by inhibiting bone resorption and agents that have a resorptive effect on bone. These include PTH, vitamin D metabolites and vitamin A. The most active vitamin D metabolite is 1,25(OH)2D. In calcium deficiency more 1,25(OH)2D is produced, causing enhanced intestinal absorption and renal absorption of calcium, and increased bone formation as well as resorption. The 1 % extra skeletal calcium is found in extracellular fluids, intracellular structures, and cell membranes.
Metabolism:
Calcium has a structural role in bone and teeth. Bone calcium is relied upon to maintain ECF calcium concentrations, which in turn are necessary for normal neuromuscular and other functions. The extracellular calcium plays an essential role in such vital functions as nerve conductance, muscle contraction, blood clotting, and membrane permeability.
Excretion:
Calcium is excreted in approximately equal amounts in urine and endogenous secretions. Calcium loss from the skin is only 0,4 mmol per day (15 mg per day), although this will increase substantially with increased sweating.

5.3. Preclinical safety data

There is no specific study with this product but the preclinical safety of the individual components has been extensively documented.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Microcrystalline cellulose,
Hydroxypropyl methylcellulose,
Glycerin monostearat GMS,
Sodium croscarmellose,
Magnesium stearate,
Silicon dioxide,
Iron oxide brown, and
Iron oxide yellow.

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at or below 25°C.

6.5. Nature and contents of container

Triple layer tablets packed in PVDC/PVC blister tray sealed with aluminium foil containing 30 tablets. Each tray is packed in a printed carton (folding carton), possibly with a leaflet enclosed.

6.6. Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Bayer (Pty) Ltd
Collaboration Hub,
1st Floor, Waterfall Circle
9 Country Estate Drive
Waterfall City
Midrand, 2090
South Africa
Co Reg. no.: 1968/011192/07
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8. REGISTRATION NUMBER(S)

To be confirmed upon registration.

9. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

To be confirmed upon registration.

10. DATE OF REVISION OF TEXT

11. DATE OF FIRST AUTHORISATION/ RENEWAL OF THE AUTHORISATION

To be confirmed upon registration.

Manufacturer:
S.I.I.T. srl Via Ariosto 50/60 20090 Trezzano S/N Milano, Italy