PROFESSIONAL INFORMATION

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

SCHEDULING STATUS
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1. NAME OF THE MEDICINE
RADICAL® TABLETS, tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains:

Active Ingredients	Elemental quantity per tablet	% NRV#
K2D3™ complex	70,0 µg	
Providing		
Vitamin D3 (*Cholecalciferol*)	1000 IU (25 µg)	167 %
Vitamin K2 (*Menaquinone*)	45 µg	38 %
Calcium (*as Calcium carbonate*)	600,0 mg	46 %
Magnesium (*as Magnesium oxide*)	100,0 mg	24 %
Copper (*as copper chelate*)	0,5 mg	56 %
Manganese (*as manganese chelate*)	0,5 mg	22 %
Zinc (*as Zinc gluconate*)	4,35 mg	40 %

Nutrient Reference Values for adults and children 4 years and older.

RADICAL® TABLETS are sugar free.

Contains sweeteners: mannitol (80 mg/tablet); sorbitol (45,69 mg/tablet).

For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM
Tablets.

White, oblong tablet.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
RADICAL® TABLETS helps maintain healthy bones and teeth. K2D3™ complex supports optimal calcium absorption. **RADICAL® TABLETS** helps to lower your risk of bone mineral loss and osteoporosis – where the bones become brittle and fragile.

4.2 Posology and method of administration
Posology:
Adults and children 12 years and older:
One (1) tablet in the evening, after a meal, with a glass of water.

Children under 12:
RADICAL® TABLETS must not be given to children under 12 years old.

RADICAL® TABLETS should be taken apart from certain foods such as bran as it may reduce the absorption of this health supplement. Certain foods e.g. those containing oxalic acid (e.g. spinach and rhubarb), phosphate (e.g. bran) or phytic acid (e.g. whole cereals) may reduce the absorption of **RADICAL® TABLETS.** See Section 4.5.

Method of administration:
For oral use only.

4.3 Contraindications
RADICAL® TABLETS are contraindicated in:
- patients who are hypersensitive to the active substances, vitamin D3, vitamin K2, calcium, magnesium, copper, manganese, zinc, or to any of the excipients listed in section 6.1.
- patients with renal impairment, chronic renal failure or renal calculi.
- patients with hypercalcaemia
- patients with sarcoidosis.
- patients taking anticoagulants such as warfarin.
- patients with porphyria.

RADICAL® TABLETS is contraindicated in combination with:
- Thiazide diuretics
- Corticosteroids, as it decreases absorption of calcium.
- Cardiac glycosides, such as digitalis.
- Orlistat, which may disturb the absorption of fat-soluble vitamins e.g. vitamin D3.
- Anticoagulants: Vitamin K decreases the effectiveness of anticoagulants. Individuals taking anticoagulants must not take this medication.
- Some anti-epileptic medicines (such as carbamazepine, phenobarbital, phenytoin and primidone), rifampicin, isoniazid and corticosteroids may reduce the effectiveness of vitamin D3.

See Section 4.5.

4.4 Special warnings and precautions for use
A doctor must be consulted if one or more of the following is applicable:
- Renal problems for example renal calculi, or heart disease or patients with an increased risk of organ damage.
- When taking any other medicines containing vitamin D or calcium. This may increase the blood level of calcium above safe levels which may cause side effects.
- If the patient suffers from sarcoidosis.
- Plasma phosphate and calcium concentrations should be monitored at regular intervals in patients with renal impairment.

Special care must be taken when taking **RADICAL® TABLETS** with other medicines, and in particular tetracyclines and some fluoroquinolones, bisphosphonates, fluoride, iron, levothyroxine, zinc and strontium ranelate. These medicines should not be taken at the same time as **RADICAL® TABLETS** Refer to section 4.5.

4.5 Interaction with other medicines and other forms of interaction
- Do not take **RADICAL® TABLETS** in combination with the following medicines: Thiazide diuretics, corticosteroids, cardiac glycosides (such as digitalis), orlistat, anticoagulants, anti-epileptics (such as carbamazepine, phenobarbital, phenytoin and primidone), rifampicin and isoniazid.
- Tetracyclines, and certain fluoroquinolones, should be taken at least 2 hours before or 4-6 hours after intake of **RADICAL® TABLETS**. Calcium carbonate may interfere with the absorption of these antibiotic preparations if taken at the same time.
- Bisphosphonates, fluoride and iron, doses should be separated by three hours.
- Calcium can reduce the effect of levothyroxine (used to treat thyroid deficiency). For this reason, levothyroxine should be taken at least four hours before or four hours after RADICAL® TABLETS.
- Calcium salts may decrease the absorption of iron, zinc and strontium ranelate. Thus, these preparations should be taken at least two hours before or after this supplement

4.6 Fertility, pregnancy and lactation
RADICAL® TABLETS is safe for use during pregnancy and breastfeeding, but a Healthcare professional should be consulted for advice.

4.7 Effects on ability to drive and use machines
No studies on the effect of **RADICAL® TABLETS** on the ability to drive or operate machinery were performed. It is unlikely that **RADICAL® TABLETS** would affect your ability to drive or use machinery. Patients should not drive or operate machinery until it is established that their ability to perform such activities has not been affected.

4.8 Undesirable effects
Immune system disorders:
Frequency unknown: angioedema or laryngeal oedema

Gastrointestinal disorders:
Frequent: constipation, winds
Less frequent: abdominal discomfort, diarrhoea, nausea.

Renal and urinary disorders:
Less frequent: Formation of renal calculi.

Reporting of suspected adverse reactions
Reporting of 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 providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
In overdose, side effects can be precipitated and/or be of increased severity. Refer to Section 4.8.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
D.34.12 Complementary Medicines: Health Supplements - Multiple substance formulation

RADICAL® TABLETS contain calcium, vitamin D3, vitamin K2, copper, magnesium, manganese and zinc.

Calcium is vital in cell signalling, muscular contractions, and is essential for the development and maintenance of strong bones and teeth. Low calcium intake may also be a risk factor in the development of osteoporosis. Many enzymes require calcium ions as a cofactor, those of the blood-clotting cascade being notable examples. Extracellular calcium is also important for maintaining the potential difference across excitable membranes, as well as proper bone formation.

Vitamin K2 plays an important role as a co-factor in the function of proteins such as osteocalcin, which is important for bone development.

Adequate intake of vitamin D is required for optimal absorption, transport and utilisation of calcium. Vitamin D deficiency has been shown to cause the mineralisation defects that result in rickets among children and osteomalacia among adults.

Magnesium is essential as a constituent of skeletal structures and in maintaining cell integrity and fluid balance and also contributes to the development of bones and teeth, as well as tissue formation.

Traces of copper are essential for the body as constituents of enzyme systems are involved in oxidation reactions. Copper thus helps to produce and repair connective tissue

Zinc is utilised in DNA synthesis and cell division and is a constituent of many enzymes. It plays a role in connective tissue formation and helps to maintain immune function and good health.

Manganese is a constituent of enzyme systems including those involved in lipid synthesis, the tricarboxylic acid cycle and purine and pyrimidine metabolism. It is bound to arginase and activates many enzymes of the liver. It also contributes to the development of normal bones.

5.2 Pharmacokinetic properties
Calcium is absorbed mainly from the small intestine by active transport and passive diffusion. Vitamin D-dependant Ca^{2}+ transport occurs in the proximal duodenum, whereas as most Ca^{2}+ uptake is mediated by passive absorption throughout the small intestine. When calcium intake is adequate or high, passive calcium absorption in the jejunum and ileum is the major absorptive process. Conversely, when intake is low, vitamin D-dependant active calcium absorption is up-regulated in the duodenum and accounts for the larger proportion of calcium that is absorbed. Calcium absorption is affected by several factors. It varies based on age, environmental and dietary conditions as well as race.

Calcium is excreted in the urine and faeces. Calcium excretion in urine is decreased when intakes of calcium are low and protein intakes are higher. In elderly individuals, faecal excretion of calcium is decreased when protein levels are increased. Age may impact the effects of protein on calcium excretion.

Vitamin D3 or Cholecalciferol is absorbed from the gastro-intestinal tract into the circulation and is subject to entero-hepatic circulation. Vitamin D metabolites are bound to specific plasma proteins.

Magnesium salts are poorly absorbed from the gastro-intestinal tract and are excreted in both urine and the faeces, with excretion reduced in deficiency states.

Manganese is poorly absorbed.

Zinc is poorly absorbed from the gastro-intestinal tract. It is widely distributed throughout the body. It is excreted in the faeces with trace amounts appearing in the urine.

5.3 Preclinical safety data
Not applicable.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
colloidal silicon dioxide;
magnesium stearate;
mannitol;
sodium starch glycolate;
stearic acid;
sorbitol

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Store at or below 25 °C.
Keep bottle tightly closed and protect from light and moisture.
Store in original packaging until required for use.

6.5 Nature and contents of container
White HDPE container and red screw-on cap, containing 30 or 60 tablets, packed in an outer carton

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Nativa (Pty) Ltd.
260 Cradock Avenue, Lyttelton, Centurion, 0157, Gauteng, South Africa
Tel: +27 (0) 12 664 7110
Customer care line: **0860 628 482**
E-mail: health@nativa.co.za
Website: www.nativa.co.za

8. REGISTRATION NUMBER
To be allocated.

9. DATE OF FIRST AUTHORISATION
To be allocated

10. DATE OF REVISION OF THE TEXT