The Real Thing Bone Revolution Capsules

Complementary Medicine. Health Supplement.

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

THE REAL THING BONE REVOLUTION CAPSULES contain Aquamin F® (calcium and magnesium) 445 mg, magnesium citrate 235 mg, boron amino acid chelate 22 mg, zinc citrate 12 mg, selenium amino acid chelate 10 mg, manganese gluconate 8 mg, MenaQ7® 10 mg (vitamin K2 0,02 mg), vitamin D3 5 microgram (200 IU) per capsule.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

THE REAL THING BONE REVOLUTION CAPSULES contain:

	Per capsule	Per 3 caps
Aquamin F® (*Lithothamnium calcareum*) [cytoskeleton]**	445 mg	1335 mg
*Providing calcium	141 mg	423 mg
*Providing magnesium	9,2 mg	27,6 mg
Magnesium citrate	235 mg	705 mg
*Providing magnesium	26,9 mg	80,7 mg
Boron amino acid chelate	22 mg	66 mg
*Providing boron	0,96 mg	2,88 mg
Zinc citrate	12 mg	36 mg
*Providing zinc	3,58 mg	10,74 mg
Selenium amino acid chelate	10 mg	30 mg
*Providing selenium	18,4 microgram	55 microgram
Manganese gluconate	8 mg	24 mg
*Providing manganese	0,77 mg	2,31 mg
MenaQ7® (Menaquinone)	10 mg	30 mg
*Providing Vitamin K2 (0,2 %)	20 microgram	60 microgram
Cholecalciferol (Vitamin D3)	2,4 mg	7,2 mg
*Providing Vitamin D (100000 IU/g)	5 microgram (200 IU)	15 microgram (600 IU)

* Elemental quantities calculated.
** Aquamin F® consists of mineralised red algae of the *Lithothamnium sp.*
The inactive ingredients include magnesium stearate (vegetable origin), vegetable (hypromellose) capsule shell. The capsules are sugar free.
For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

THE REAL THING BONE REVOLUTION CAPSULES is a clear, hard vegetable capsule, size 00, containing a fine cream coloured powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

THE REAL THING BONE REVOLUTION CAPSULES is a health supplement –

- Source of calcium and magnesium (Aquamin F ®), with added vitamins and minerals that increase the intestinal absorption of calcium and phosphorous, all playing an important role in the development and maintenance of bones.
- Calcium when combined with sufficient vitamin D, a healthy diet and regular exercise, may reduce the risk of developing osteoporosis and are beneficial for the prevention of bone loss and fractures.

Supplementation should not replace a healthy, balanced and varied diet.

4.2 Posology and method of administration

Adults 18 years and older: Take 3 (three) capsules orally once a day with a glass of water or consult your healthcare practitioner. Take after low-fibre foods to avoid faster rate of intestinal transit. Avoid phytates as it reduces zinc absorption, see section 5.2. Take with meals to reduce gastrointestinal effects.
Avoid taking more than 1 300 mg calcium per day; consider all sources, dietary and supplementation (count approximately 300 mg/day from non-dairy foods and 300 mg/day per cup of milk).
Gastrointestinal adverse effects are particularly common if zinc salts are taken on an empty stomach, and may be reduced by giving them with meals.

Paediatric population

THE REAL THING BONE REVOLUTION CAPSULES is not indicated in paediatrics. The safety in children up to age 18 years has not been established. It is not suitable for use in children.

4.3 Contraindications

Hypersensitivity to any of the ingredients.
High doses of calcium salts should be avoided in patients with calcium renal calculi or a history of renal calculi.
Vitamin D is contraindicated if there is hypercalcemia.

4.4 Special warnings and precautions for use

Use calcium with caution if the patient has kidney impairment or diseases associated with hypercalcaemia such as sarcoidosis and some malignancies. Patients with achlorhydria should take calcium with a meal to increase absorption. Smoking decreases calcium intestinal absorption. Diets high in caffeine, sodium or protein may increase urinary excretion of calcium. Kidney disease reduces magnesium excretion and increases the risk for hypermagnesemia; use cautiously. Magnesium salts can cause a false increase in serum alkaline phosphatase test results, and a false increase in serum calcium test results in some procedures using EDTA.
Long term use of proton pump inhibitors are linked to increased risk of hypomagnesaemia.
Selenium might exacerbate hypothyroidism in patients with iodine deficiency; however it does not have a significant effect on thyroid function when iodine intake is adequate.
Selenium might cause excessive bleeding if used perioperatively; it has antiplatelet effects. Discontinue selenium at least 2 weeks before elective surgery.
Chronic liver disease can lead to manganese accumulation and toxicity. Patients with iron-deficiency anaemia might have enhanced manganese absorption. Manganese salts can cause a false increase in serum alkaline phosphatase test results.

Doses of vitamin D higher than that recommended long term can lead to hypercalcaemia or hyperphosphataemia. Hypercalcaemia can contribute to arteriosclerosis, particularly in patients with kidney disease. Vitamin D should be used with caution in patients with renal impairment or calculi, or heart disease, who might be at increased risk of organ damage if hypercalcaemia occurs. Plasma phosphate concentrations should be controlled during vitamin D therapy.
Vitamin D may increase calcium levels in patients with histoplasmosis, with increased risk of complications such as kidney stones and calcified tissue.
Vitamin D may increase calcium levels and lead to hypercalcaemia in patients with hyperparathyroidism, lymphoma, sarcoidosis and tuberculosis with increased risk of complications such as kidney stones and calcified tissue. Vitamin D may increase calcium levels and increase risk of arteriosclerosis in patients with renal failure.
Vitamin D may cause increased lab values of urinary and blood calcium, phosphate, albumin, blood urea nitrogen, serum cholesterol, aspartate aminotransferase and alanine aminotransferase.
Aquamin F® contains traces of iodine at 4,24 ppm.

4.5 Interaction with other medicines and other forms of interaction
Other medicines affecting THE REAL THING BONE REVOLUTION CAPSULES:
Thiazide diuretics reduce urinary excretion of calcium, which could lead to hypercalcaemia or renal failure if vitamin D (which increases absorption of calcium) or large doses of calcium is taken concurrently.
Loop diuretics or large doses of aluminium might increase calcium excretion and calcium requirements.
Carbamazepine, phenobarbital, phenytoin or mineral oil decrease calcium absorption and increase calcium requirements. After 6 months of carbamazepine, phenobarbital or phenytoin these patients may need vitamin D and calcium supplementation. Advise patients against regular or long term use of mineral oil.
Corticosteroids might increase calcium requirements. These patients may need vitamin D plus calcium supplementation.
Stimulant laxatives might decrease calcium absorption and increase calcium requirements. Advise patients to use these laxatives short term.
Calcium and tetracycline antibiotics bind together and reduce each other's absorption. Take tetracyclines at least 2 hours before or 4-6 hours after calcium supplements or calcium-containing foods.
A low fat, high fibre (bran) diet reduces the gastrointestinal absorption and increases excretion of calcium.
Potassium-sparing diuretics and boron decrease excretion of magnesium, possibly increasing magnesium levels.
Aminoglycoside antibiotics and amphotericin B can cause nephrotoxicity which causes increased urinary loss of electrolytes such as magnesium.
Cetuximab, corticosteroids, digoxin, some diuretics, panitumumab, pentamidine and tacrolimus cause increased loss of magnesium in the urine. Cyclosporine and capecitabine may damage renal tubules and increase magnesium losses in the urine.
Oestrogens reduce serum levels of magnesium by increasing its uptake into body tissues.
Foscarnet can increase removal of magnesium from the body, causing symptomatic hypomagnesemia.
Penicillamine can reduce magnesium absorption by chelating magnesium in the gut.
High doses of sodium phosphates deplete magnesium.
Deferoxamine, EDTA in propofol, and thiazide diuretics increase urinary excretion of zinc and might decrease zinc levels.

Iron supplements, penicillamine, phosphorus-containing preparations and tetracyclines may reduce the absorption of zinc.
Calcium and iron can decrease manganese absorption. Zinc can increase manganese absorption and plasma levels.
Coenzyme Q10 has vitamin K-like activity and may have additive effects such as increased risk of blood clotting in people taking anticoagulants.
Large doses of vitamin E might block the effects of vitamin K, increasing the risk of bleeding in patients who are taking warfarin.
Prolonged therapy with antibiotics might decrease levels of vitamin K, which could result in prolonging clotting times and increasing bleeding risk.
Calcipotriene taken with vitamin D increases the risk for hypercalcaemia.
Orlistat decreases absorption and blood levels of vitamin D. Separate the dosing time by at least 2 hours.

THE REAL THING BONE REVOLUTION CAPSULES affecting other medicines:
Calcium salts reduce the absorption of bisphosphonates, sotalol, tetracycline antibiotics, fluoroquinolone antibiotics and quinoline antibiotics; take medication at least 2 hours before or 4-6 hours after calcium supplements.
Calcium reduces levels of dolutegravir, elvitegravir and levothyroxine; take medication at least 2 hours before or 4-6 hours after calcium supplements.
Calcium supplementation may decrease the absorption of dietary iron, zinc and magnesium, therefore take calcium supplements at bedtime.
Calcium enhances the effects of digitalis glycosides on the heart.
Calcium salts reduce the absorption of fluoride; doses should be separated by at least 3 hours.

Magnesium can decrease the absorption of bisphosphonates and tetracyclines; separate doses by at least 2 hours.
Magnesium can form insoluble complexes with quinolones and decrease their absorption; advise persons to take quinolones at least 2 hours before, or 4-6 hours after magnesium.
Boron might increase levels of magnesium.
Zinc at high levels might reduce the absorption of magnesium.
Zinc can decrease the levels and clinical effects of penicillamine, quinolone antibiotics, tetracycline antibiotics and iron. Take at least 2 hours before, or 4-6 hours after zinc.
Selenium may have antiplatelet effects and may increase the risk of bleeding if used with anticoagulant or antiplatelet drugs, or other products that have antiplatelet activity.

Vitamin K can antagonize and reverse the therapeutic effects of warfarin; large doses of vitamin K can reduce the anticoagulant effect of warfarin.
Vitamin D in high doses can increase magnesium absorption.
Vitamin D increases the absorption of calcium in the small intestine; excessive amounts of vitamin D might increase the risk of hypercalcaemia. Hypercalcaemia induced by high-doses of vitamin D can reduce the therapeutic effects of verapamil for arrhythmia.
There is an increased risk of hypercalcaemia if vitamin D is given with thiazide diuretics, calcium or phosphate.

4.6 Fertility, pregnancy and lactation
Advise the patient to consult a healthcare practitioner prior to use if she is pregnant or breastfeeding. When magnesium is used in pregnant women, foetal heart rate should be monitored and use within 2 hours of delivery should be avoided. No fertility data is available.

4.7 Effects on ability to drive and use machines
THE REAL THING BONE REVOLUTION CAPSULES may have a minor influence on the ability to drive and use machines due to possible undesirable effects.

4.8 Undesirable effects
a. Summary of the safety profile
General reactions to multivitamin-mineral combinations include possible gastrointestinal effects and hypersensitivity reactions.

b. List of adverse reactions
Side effects for the combination have not been documented. The following effects have been documented for the active ingredients:

Blood and lymphatic system disorders
- Hypercalcaemia (rare), usually in patients with impaired renal function or in those also taking vitamin D.
- Hypermagnesaemia is uncommon, except in patients with renal impairment.

Nervous system disorders
Headache (common).
Eye disorders
Visual impairment or nystagmus (rare).
Cardiac disorders
Calciphylaxis resulting in skin ulcers and skin necrosis (rare). Myocardial infarction. Rapid heartbeat when administered antenatally.
Gastrointestinal disorders
Gastrointestinal discomfort, gastrointestinal irritation, gastritis, abdominal cramping or pain, belching (common), flatulence (common), nausea (common), vomiting (common), diarrhoea (common), metallic taste due to zinc (common), dyspepsia/indigestion, heartburn, mouth irritation, dry mouth.
Skin and subcutaneous tissue disorders
Hypersensitivity reactions, allergic skin rash (rare), skin and skin appendage lesions.
Reproductive system and breast disorders
Vaginal discharge and itching.

Frequencies of all adverse events are not known.

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. Healthcare practitioners 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

Alternatively, suspected adverse reactions may be reported directly to the Holder of the Certificate of Registration, The Real Thing Food Supplements (Pty) Ltd at telephone 021-701 0244 or e-mail adr@therealthing.co.za

4.9 Overdose

With an overdose, side effects can be precipitated and/or be of increased severity.
Excess calcium in the presence of renal failure or in those also taking vitamin D may lead to hypercalcaemia. Symptoms of excess calcium include kidney stones, hypercalciuria, milk-alkali syndrome, hypercalcaemia (symptoms of hypercalcaemia include anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, nephrocalcinosis, renal calculi, and in severe cases cardiac arrhythmias and coma).
Diarrhoea may occur with large doses of magnesium. Symptoms of magnesium toxicity include thirst, hypotension, CNS depression, drowsiness, confusion, skeletal muscle paralysis, loss of tendon reflexes, respiratory depression, cardiac arrhythmias, coma, cardiac arrest and death. Renal insufficiency increases the likelihood of toxicity due to hypermagnesaemia.
Large doses of boron can cause persistent gastrointestinal symptoms. Large doses of boron can result in acute poisoning with symptoms of hyperexcitability, irritability, tremors, convulsions, weakness, lethargy and headaches.

Zinc overdose and toxicity include zinc-induced copper deficiency, acute tubular necrosis (rare) and interstitial nephritis (rare). In acute over dosage zinc salts are corrosive. Large amounts of zinc can result in irritation and corrosion of the gastrointestinal tract, watery diarrhoea, epigastric pain and severe vomiting. Zinc toxicity include vomiting, dehydration, poor muscle coordination, dizziness and abdominal pain.
Over dosage of selenium has been associated with loss of hair, nail changes, nausea, vomiting, diarrhoea, weight loss, dermatitis, metallic taste, garlic odour of breath, irritability, fatigue and peripheral neuropathy.

Acute selenium poisoning may cause fever, gastrointestinal symptoms (nausea, vomiting, pain, anorexia), liver or kidney functional impairment, muscle tenderness, tremor, facial flushing, respiratory distress or cardiac complications. Also restlessness, hypersalivation, muscle spasm, haemolysis, liver necrosis, cerebral and pulmonary oedema, coma and death.
Chronic exposure to high amounts of selenium has been reported to cause toxic effect on endocrine function, hepatotoxicity, gastrointestinal disturbances and dermatological effects such as nail and hair loss, dermatitis.

Excessive doses of vitamin D can lead to vitamin D intoxication with symptoms of hypertension (rare), pancreatitis, osteoporosis, calcific conjunctivitis and photophobia, psychosis (rare), runny nose, azotemia (rare), anaemia, weight loss, anorexia, metastatic calcification, generalized vascular calcification, hypercalcaemia with kidney stones or kidney insufficiency, seizures, increased risk of certain types of cancer. Symptoms of renal impairment include frequency, night time awakening to urinate, thirst, inability to concentrate urine, proteinuria and is usually reversible with discontinuing vitamin D supplements.
Vitamin D overdose can lead to hyperphosphatemia or hypercalcaemia. Associated effects of hypercalcaemia include hypercalciuria, ectopic calcification, and renal and cardiovascular damage. Symptoms of vitamin D over dosage include anorexia, lassitude, nausea and vomiting, constipation or diarrhoea, polyuria, nocturia, sweating, headache, thirst, somnolence and vertigo.

In the event of overdose, advise the patient to stop taking the supplement. Treatment of over dosage is symptomatic and supportive. Treatment of zinc over dosage consists of giving milk or alkali carbonates and activated charcoal; do not use emetics or gastric lavage due to the corrosive action of zinc.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

THE REAL THING BONE REVOLUTION CAPSULES belongs to category D Complementary Medicines, Health Supplements, class 34.12 Multiple Substance Formulation.
As a multi-vitamin/ mineral supplement it contributes to the maintenance of overall good health and optimal bone health that depends on bone mineral content and bone quality.

THE REAL THING BONE REVOLUTION CAPSULES is a specifically formulated, bone-related supplement containing calcium and magnesium (Aquamin F®), boron, zinc, selenium, manganese, vitamin K2 and vitamin D3 to assist with maintenance of optimal bone health and for those at risk of low nutrient intake. It is a supplement that helps improve the levels of specific nutrients in the body involved in optimal, healthy bone turnover, nutrient-deficiency-related bone loss and fractures. Calcium combined with vitamin D helps reduce bone loss in people, as well as in those taking bone-reducing medication such as corticosteroids.
Oral calcium treats and prevents hypocalcaemia. Calcium is essential for normal bone structure and function.
Oral magnesium treats hypomagnesemia. During magnesium deficiency bone resorption takes place which releases calcium and magnesium from bone. Magnesium is important for normal bone structure. Magnesium increases bone mineral density and decreases bone loss in postmenopausal patients, and in postmenopausal patients with osteoporosis.
It is suggested that adequate intakes of magnesium alone, or in combination with calcium, vitamin D and zinc reduces bone turnover, and increases bone density. High doses of vitamin D can increase magnesium absorption.
Boron, as well as other trace minerals, play important roles in the development and maintenance of bone. Boron may increase calcium absorption and decrease urinary loss of calcium and magnesium.

Zinc is a biologically essential trace element. Oral zinc is effective for treating and preventing zinc deficiency. It is used as a co-factor in bone mineralization.
Selenium is an essential trace mineral with antioxidant activity. Oral selenium is effective for the treatment and prevention of selenium deficiency.
Manganese is an essential nutrient. It acts as a cofactor in several metabolic and enzymatic reactions. Oral manganese is effective for preventing and treating manganese deficiency. Manganese contributes to the development and maintenance of normal bones. It might have a role in osteoporosis; decreased plasma manganese concentrations have been linked to osteoporosis, and bone mineral density seems to improve when trace minerals including manganese are added to calcium supplementation.
Vitamin K refers to a group of fat soluble compounds, of which vitamin K2 is called menaquinones. Vitamin K2 might reduce the risk of fractures and bone loss in patients with osteoporosis. Vitamin K2 is a cofactor for carboxylation of the proteins such as osteocalcin required for strong bone and cartilage.

Vitamin D is an essential fat-soluble vitamin. Vitamin D3 (cholecalciferol) is more potent than vitamin D2 (ergocalciferol). Vitamin D3 is metabolized in the body to its active metabolite, calcitriol.
Oral vitamin D prevents and treats vitamin D deficiency. The main function of vitamin D is to regulate serum calcium and phosphorus concentrations and bone mineralisation. Regular intake of oral vitamin D with calcium helps to prevent the progression of osteoporosis; it might also reduce the risk of fracture in some patients. Vitamin D facilitates the intestinal absorption of calcium. Calcium and vitamin D work synergistically in the prevention of bone loss and fractures.

5.2 Pharmacokinetic properties

Calcium is absorbed mainly from the small intestine. Excess calcium is mainly excreted renally. Unabsorbed calcium is eliminated in the faeces, together with that secreted in the bile and pancreatic juice. Calcium crosses the placenta and is distributed into breast milk.
The bones and teeth contain greater than 99 % of the calcium in the human body. It is also present in blood, extracellular fluid, muscle and other tissues. Calcium in bone serves as the reserve source of calcium. Half of serum calcium is bound to plasma proteins whereas the free or ionised calcium serves as the clinical indicator of calcium status.
Magnesium requires both parathyroid hormone and vitamin D for absorption. About one-third of dietary magnesium is absorbed from the small intestine; the fraction absorbed increases as the magnesium store decreases. Body stores are divided between skeleton and soft tissue. One third of skeletal magnesium acts as a reservoir to maintain extracellular magnesium concentrations. Magnesium is excreted primarily via the kidneys. Small amounts of magnesium are distributed into breast milk. Magnesium crosses the placenta.

Boron distributes to all tissues, with the highest concentration in bone and the lowest in adipose tissue. It is not well metabolised as greater than 90 % of the dose is excreted unchanged. When taken orally, boron is excreted unchanged in the urine.
Absorption of zinc increases in states of zinc deficiency and if zinc intakes are low. Zinc is mostly absorbed in the small intestine, and is reduced in the presence of phytates (tubers, legumes, seeds, nuts, unprocessed whole grains (such as whole wheat, oats, rice)). More than 85 % of the total zinc in the body is in skeletal muscle and bone. Metabolism takes place in the liver. Zinc is primarily excreted in faeces, while small amounts are lost in urine and perspiration. During lactation, zinc excretion increases via breast milk.
Approximately 80 % of dietary selenium is absorbed. Selenium travels via the gastrointestinal tract, crosses the intestinal barrier, reaches the blood circulation, and is distributed to different tissues of the body. It is stored in red blood cells, the liver, spleen, heart, nails and skin. The kidney accumulates the highest level of selenium in the body. It is metabolised to its active form in tissues. Selenium is excreted in urine, and to a lesser extent in faeces.
Absorption of manganese from the gastrointestinal tract is variable. Absorbed manganese accumulates in tissue, including bone, where it can remain for many years. It is excreted hepatically, hence chronic liver disease and biliary disorders can cause manganese accumulation and toxicity.

Vitamin K2 is well absorbed. Bile salts are required for absorption from the gastrointestinal tract. Vitamin K2 is transported with LDL and triacylglycerol-rich fractions of plasma lipoproteins, reaching the liver and many extrahepatic tissues.
Vitamin K accumulates mainly in the liver but is stored in the body for only short periods of time. Vitamin K does not appear to cross the placenta readily and it is variably distributed into breast milk. Vitamin K is excreted in urine and faeces.
Vitamin D substances are well absorbed from the gastrointestinal tract. The presence of bile is essential for adequate intestinal absorption; absorption may be decreased in patients with decreased fat absorption. It is transported primarily by chylomicron, which allows vitamin D to be distributed to peripheral tissues. Vitamin D can be stored in adipose tissue and muscle tissue for long periods of time. It is slowly released from such storage sites and from the skin where it is formed in the presence of sunlight or ultra-violet light. Vitamin D3 (cholecalciferol) is biologically inert. If not taken up by peripheral tissue, it is converted to calcitriol. It is hydroxylated in the liver and thereafter in the kidneys to its active form, calcitriol. People with chronic renal failure may require forms of vitamin D (such as calcitriol) that do not require hydroxylation.

Vitamin D and its metabolites are excreted mainly in the bile and faeces, with only small amounts appearing in the urine.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The inactive ingredients include:

- magnesium stearate (vegetable origin)
- vegetable (hypromellose) capsule shell.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

THE REAL THING BONE REVOLUTION CAPSULES has a shelf life of 2 years when stored in a cool, dry place at or below 25 °C.

6.4 Special precautions for storage

Store in an airtight container, protected from light.

6.5 Nature and contents of container

THE REAL THING BONE REVOLUTION CAPSULES are packed in a 200 ml amber glass bottle with a child resistant 45 mm polyethylene black screw cap fitted with an aluminium foil heat-induction or pressure tamper-evident seal. A silica gel sachet is included in the bottle. The bottle contains 90 capsules.

6.6 Special precautions for disposal

No special requirements.

7 HOLDER OF CERTIFICATE OF REGISTRATION

The REAL THING FOOD SUPPLEMENTS (PTY) LTD
9 Westlake Drive
Westlake 7945, Cape Town
Telephone: 021-701 0244
E-mail: info@therealthing.co.za

8 REGISTRATION NUMBER

(To be allocated)

9 DATE OF FIRST AUTHORISATION

(To be allocated)

10 DATE OF REVISION OF THE TEXT

30/11/2023.