MECURE INDUSTRIES PLC

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

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1. Name of the medicinal product

ZEVIT FOR MEN (Am Capsules/Pm Tablets).

2. Qualitative and quantitative composition

Zevit AM:

Each Liqui- Capsule Contains:

Oil Component:

Vitamin A Palmitate	BP	2000IU
Vitamin D3	BP	200IU
Vitamin K	BP	0.12mg
Vitamin E	BP	15mg
Lutein (10% extract)	BP	1mg
Lycopene	BP	0.3mg
BHA	BP	
Butylated Hydroxytoluene (BHT)	BP	
Vegetable Oil	BP	
Capsule Shell	BP	

Tablet Component:

Vitamin C	BP	99mg
Vitamin B6 (Pyridoxine)	BP	1.519mg
Vitamin B1 (Thaimine)	BP	0.924mg
Vitamin B2 (Riboflavin)	BP	1.001mg
Folic Acid	BP	0.168mg
Vitamin B12	BP	4.368mcg
Copper (as Copper Sulphate)	BP	0.630mg
Potassium (as Potassium Iodide)	BP	0.105mg
Selenium (as Selenium Dioxide)	BP	0.0835mg
Niacinamide	BP	12.32mg
Biotin (Vitamin B7)	BP	0.0301mg
Pantothenic Acid	BP	10.85mg
Manganese (as Manganese Oxide)	BP	2.3mg
Chromium (as Chromium Chloride)	BP	0.0245mg

For the full list of excipients, see section 6.1.

Zevit PM:

Each Film Coated Tablet contains:

Calcium (as Calcium Carbonate)	BP	21mg
Magnesium (as Magnesium Sulphate)	BP	25mg
Zinc (as Zinc Oxide)	BP	11mg
Isoleucine	BP	10mg
Leucine	BP	15mg
Valine	BP	25mg

Vitamin B6 (Pyridoxine)	BP	0.651mg
Vitamin B1 (Thaimine)	BP	0.396mg
Vitamin B2 (Riboflavin)	BP	0.429mg
Folic Acid	BP	0.072mg
Vitamin B12	BP	1mcg
Copper (as Copper Sulphate)	BP	0.27mg
Iodine (as Potassium Iodide)	BP	0.045mg
Selenium (as Selenium Dioxide)	BP	0.0165mg
Niacinamide (Vitamin D3)	BP	5.28mg
Biotin (Vitamin B7)	BP	0.0129 mg
Pantothenic Acid (Vitamin B5)	BP	4.65mg
Manganese (as Manganese Oxide)	BP	0.69 mg
Chromium (as Chromium Chloride)	BP	0.0105mg

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Zevit AM:
Liqui-tab Capsule.
Transparent cap and body hard gelatin capsule printed “Zevit” on cap containing red coloured oblong shaped film coated tablet and oil.

Zevit PM:
Film Coated Tablet.
Dark blue coloured oblong shaped film coated tablet embossed with “Zevit” and “PM” on either side.

4. Clinical particulars

4.1 Therapeutic indications

Healthy body, good appetite, convalescence. All conditions where there is need for vitamins to withstand stress and increased demands.

4.2 Posology and method of administration

Posology:
1 Capsule of Zevit AM in the morning & 1 Tablet of Zevit PM in the evening;
or as directed by a physician.

Method of administration: Oral

4.3 Contraindications

Hypercalcaemia, haemochromatosis and other iron storage disorders.

Hypersensitivity to the active substance(s) or to any of the excipients.

Zevit AM & PM for women contain vegetable oil. Patients allergic to vegetable oil should not take this medicine.

4.4 Special warnings and precautions for use

Whilst taking Zevit AM & PM for men both protein and energy are also required to provide complete nutrition in the daily diet.

Patients with thyroid disorders should seek medical advice before taking Zevit AM & PM for women. An allowance should be madefor vitamins or minerals obtained from other sources.

4.5 Interaction with other medicinal products and other forms of interaction

Folic acid can reduce the plasma concentration of phenytoin. Oral iron and Zinc Oxide reduce the absorption of tetracyclines.

4.6 Effects on ability to drive and use machines

None anticipated.

4.7 Undesirable effects

Assessment of undesirable effects is based on the following frequency

groupings:

Very common: ≥ 1/10

Common: ≥ 1/100 to <1/10

Uncommon: ≥ 1/1,000 to

<1/100Rare: ≥ 1/10,000 to

<1/1,000 Very rare: <1/10,000

Not known: cannot be estimated from the available data

Immune system disorders	*Not known:* Hypersensitivity reaction (such as rash)
Gastrointestinal disorders	*Not known:* Gastrointestinal disturbances (such as nausea, vomiting and abdominal pain)

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 pharma@mecure.com.

4.8 Overdose

No cases of overdosage due to Zevit AM & PM therapy have been reported. Any symptoms which may be observed due to the ingestion of large quantities of Zevit AM & PM for men will be due to the fat soluble vitamin content. If iron overdosage is suspected, symptoms may include nausea, vomiting, diarrhoea, abdominal pain, haematemesis, rectal bleeding, lethargyand circulatory collapse. Hyperglycaemia and metabolic acidosis may also occur. Treatment should be implemented immediately. In severe cases, after a latent phase, relapse may occur after 24 - 48 hours, manifest by hypotension comaand hepatocellular necrosis and renal failure.

5. Pharmacological properties

5.1 Pharmacodynamic properties

The following account summarises the pharmacological effects of the vitamins and minerals in Zevit AM & PM for men and describes the conditions caused by deficiency of these.

Vitamin A

Vitamin A plays an important role in the visual process. It is isomerised to the 11-cis isomer and subsequently bound to the opsin to form the photoreceptor for vision under subdued light. One of the earliest symptoms of deficiency is night blindnesswhich may develop into the more serious condition xerophthalmia. Vitamin A also participates in the formation and maintenance of the integrity of epithelial tissues and mucous membranes. Deficiency may cause skin

changes resulting in a dry rough skin with lowered resistance to minor skin infections. Deficiency of Vitamin A, usually accompanied by protein-energy malnutrition, is linked with a frequency of infection and with defective immunological defence mechanisms.

Vitamin D

Vitamin D is required for the absorption of calcium and phosphate from the gastro-intestinal tract and for their transport. Itsinvolvement in the control of calcium metabolism and hence the normal calcification of bones is well documented.
Deficiency of Vitamin D in children may result in the development of rickets.

Vitamin K

Vitamin K is essential for effective blood coagulation and plays a key role in synthesising certain clotting factors found in the clotting cascade. In the liver, it acts as a co-enzyme for γ-glutamyl carboxylase, an enzyme that converts the inactive forms of factors II (prothrombin), VII, IX and X into their active forms through the carboxylation of glutamic acid residues. Vitamin K also helps synthesise Protein C and Protein S. These are important in the regulation of the clotting cascade by providing negative feedback in the form of anticoagulation. Vitamin K contributes to calcium metabolism. It is required for the synthesis of two regulatory proteins called osteocalcin and matrix Gla-protein (MGP). Osteocalcin is produced by osteoblasts and encourages bone calcification, while MGP inhibits calcification of the blood vessels. By ensuring calcium stays in the bones, Vitamin K is thought to prevent the development of osteoporosis and cardiovascular disease.

Vitamin B_1 (Thiamine)

Thiamine (as the coenzyme, thiamine pyrophosphate) is associated with carbohydrate metabolism. Thiamine pyrophosphate also acts as a co-enzyme in the direct oxidative pathway of glucose metabolism. In thiamine deficiency, pyruvic and lactic acids accumulate in the tissues. The pyruvate ion is involved in the biosynthesis of acetylcholine via its conversion to acetyl co-enzyme A through a thiamine-dependent process. In thiamine deficiency, therefore, there are effectson the central nervous system due either to the effect on acetylcholine synthesis or to the lactate and pyruvate accumulation. Deficiency of thiamine results in fatigue, anorexia, gastro-intestinal disturbances, tachycardia, irritability andneurological symptoms. Gross deficiency of thiamine (and other Vitamin B group factors) leads to the condition beri-beri.

Vitamin B_2 (Riboflavin)

Riboflavin is phosphorylated to flavin mononucleotide and flavin adenine dinucleotide which act as co-enzymes in the respiratory chain and in oxidative phosphorylation. Riboflavin deficiency presents with ocular symptoms, as well as lesionson the lips and at angles of the mouth.

Vitamin B_6 (Pyridoxine)

Pyridoxine, once absorbed, is rapidly converted to the co-enzymes pyridoxal phosphate and pyridoxamine phosphate whichplay an essential role in protein metabolism. Convulsions and hypochromic anaemia have occurred in infants deficient in pyridoxine.

Vitamin B_{12} (Cyanocobalamin)

Vitamin B_{12} is present in the body mainly as methylcobalamin and as adenosylcobalamin and hydroxocobalamin. These actas co-enzymes in the trans methylation of homocysteine to methionine; in the isomerisation of methylmalonyl co-enzyme to succinyl co-enzyme and with folate in several metabolic pathways respectively. Deficiency of Vitamin B_{12} interferes with haemopoiesis and produces megaloblastic anaemia.

Vitamin C (Ascorbic Acid)

Vitamin C cannot be synthesised by man therefore a dietary source is necessary. It acts as a cofactor in numerous biological processes including the hydroxylation of proline to hydroxyproline. In deficiency, the formation of collagen is, therefore, impaired. Ascorbic acid is important in the hydroxylation of dopamine to noradrenaline and in hydroxylations occurring in steroid synthesis in the adrenals. It is a reducing agent in tyrosine metabolism and by acting as an electrondonor in the conversion of folic acid to tetrahydrofolic acid is indirectly involved in

the synthesis of purine and thymine.
Vitamin C is also necessary for the incorporation of iron into ferritin. Vitamin C increases the phagocytic function of leucocytes; it possesses anti-inflammatory activity and it promotes wound healing. Deficiency can produce scurvy. Featuresinclude swollen inflamed gums, petechial haemorrhages and subcutaneous bruising. The deficiency of collagen leads to development of thin watery ground substances in which blood vessels are insecurely fixed and readily ruptured. The supportive components of bone and cartilage are also deficient causing bones to fracture easily and teeth to become loose.Anaemia commonly occurs probably due to Vitamin C's role in iron metabolism.

Vitamin E

Vitamin E deficiency has been linked to disorders such as cystic fibrosis where fat absorption is impaired. It is essential forthe normal function of the muscular system and the blood.

Niacinamide

The biochemical functions of Niacinamide as NAD and NADP (Niacinamide adenine dinucleotide phosphate) include the degradation and synthesis of fatty acids, carbohydrates and amino acids as well as hydrogen transfer. Deficiency producespellagra and mental neurological changes.

Calcium (Calcium Carbonate)

Calcium is an essential body electrolyte. It is involved in the maintenance of normal muscle and nerve function and essential for normal cardiac function and the clotting of blood. Calcium is mainly found in the bones and teeth. Deficiency ofcalcium leads to rickets, osteomalacia in children and osteoporosis in the elderly.

Pantothenic Acid

Pantothenic acid is incorporated into co-enzyme A and is involved in metabolic pathways involving acetylation which includes detoxification of drug molecules and biosynthesis of cholesterol, steroid hormones, mucopolysaccharides and acetylcholine. CoA has an essential function in lipid metabolism.

Folic Acid

Folic acid is reduced in the body to tetrahydrofolate which is a co-enzyme for various metabolic processes, including the synthesis of purine and pyrimidine nucleotides and hence in the synthesis of DNA. It is also involved in some amino acid conversion and in the formation and utilisation of formate. Deficiency of folic acid leads to megaloblastic anaemia.

Vitamin B7 (Biotin)

Biotin is a co-enzyme for carboxylation during the metabolism of proteins and carbohydrates.

Selenium

Selenium is an essential trace element, deficiency of which has been reported in man. It is thought to be involved in thefunctioning of membranes and the synthesis of amino acids. Deficiency of selenium in the diet of experimental animals produces fatty liver followed by necrosis.

Copper (Copper Sulphate)

Traces of copper are essential to the body as constituents of enzyme systems involved in oxidation reactions.

Magnesium (Magnesium Sulphate)

Magnesium is essential to the body as a constituent of skeletal structures and in maintaining cell integrity and fluid balance.It is utilised in many of the functions in which calcium is concerned but often exerts the opposite effect. Some enzymes require the magnesium ion as a co-factor.

Potassium (Potassium Iodide)

Potassium is the principle cation of intracellular fluid and is intimately involved in the cell function and metabolism. It is essential for carbohydrate metabolism and glycogen storage and protein synthesis and is involved in transmembrane potential where it is necessary to maintain the resting potential in excitable cells. Potassium ions maintain intracellular pHand osmotic pressure. Prolonged or severe diarrhoea may lead to potassium deficiency.

Zinc (Zinc Oxide)

Zinc is a constituent of many enzymes and is, therefore, essential to the body. It is present with insulin in the pancreas. Itplays a role in DNA synthesis and cell division. Reported effects of deficiency include delayed puberty and hypogonadal dwarfism.

Manganese (Manganese Oxide)

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 of the liver and activates many enzymes.

Iodine (Potassium Iodide)

Iodine is an essential constituent of the thyroid hormones.

Chromium (Chromium Chloride)

Chromium is an essential trace element involved in carbohydrate metabolism.

Lycopene

Lycopene is a powerful antioxidant with many health benefits, including sun protection, improved heart health and a lower risk of certain types of cancer.

Valine, Leucine, Isoleucine
Valine, Leucine and Isoleucine make up a trio of branched-chain amino acids that enhance energy, increase endurance, and aid in muscle tissue recovery and repair. This group also lowers elevated blood sugar levels and increases growth hormone production.

5.2 Pharmacokinetic properties
The following account describes the absorption and fate of each of the active constituents of Zevit AM & PM for women.

Vitamin A

Except when liver function is impaired, Vitamin A is readily absorbed. β -carotene (as in Zevit AM & PM for women) is Provitamin A and is the biological precursor to Vitamin A. It is converted to Vitamin A (Retinol) in the liver; retinol is emulsified by bile saltsand phospholipids and absorbed in a micellar form. Part is conjugated with glucuronic acid in the kidney and part is metabolised in the liver and kidney, leaving 30 to 50% of the dose for storage in the liver. It is bound to a globulin in theblood. Metabolites of Vitamin A are excreted in the faeces and the urine.

Vitamin D

The metabolism of ergocalciferol is similar to that of cholecalciferol. Cholecalciferol is absorbed from the gastro-intestinaltract into the circulation. In the liver, it is hydroxylated to 25-hydroxycholecalciferol, is subject to entero-hepatic circulationand is further hydroxylated to 1,25-dihydroxycholecalciferol in the renal tubule cells. Vitamin D metabolites are bound to specific plasma proteins.

Vitamin K

Vitamin K is absorbed through the ileum and jejunum of the small bowel. As a fat-soluble vitamin, Vitamin K is carried through the enterocytes by a large fat goblet called a micelle. Here, it enters the bloodstream via the lymphatic system.

Vitamin B_1 (Thiamine)

Thiamine is absorbed from the gastro-intestinal tract and is widely distributed to most body tissues. Amounts in excess ofthe body's requirements are not stored but excreted in the urine as unchanged thiamine or its metabolites.

Vitamin B_2 (Riboflavin)

Riboflavin is absorbed from the gastro-intestinal tract and in the circulation is bound to plasma proteins. It is widely distributed. Little is stored and excess amounts are excreted in the urine. In the body Riboflavin is converted to flavinmononucleotide (FMN) and then to flavin adenine dinucleotide (FAD).

Vitamin B_6 (Pyridoxine)

Pyridoxine is absorbed from the gastro-intestinal tract and converted to the active pyridoxal phosphate which is bound toplasma proteins. It is excreted in the urine as 4-pyridoxic acid.

Vitamin B_{12} (Cyanocobalamin)

Cyanocobalamin is absorbed from the gastro-intestinal tract and is extensively bound to specific plasma proteins. A studywith labelled Vitamin B_{12} showed it was quickly taken up by the intestinal mucosa and held there for 2 - 3 hours. Peak concentrations in the blood and tissues did not occur until 8 - 12 hours after dosage with maximum concentrations in the liver within 24 hours. Cobalamins are stored in the liver, excreted in the bile and undergo enterohepatic recycling. Part of adose is excreted in the urine, most of it in the first eight hours.

Vitamin C (Ascorbic Acid)

Ascorbic acid is readily absorbed from the gastro-intestinal tract and is widely distributed in the body tissues. Ascorbic acidin excess of the body's needs is rapidly eliminated in the urine and this elimination is usually accompanied by a mild diuresis.

Vitamin E

Vitamin E is absorbed from the gastro-intestinal tract. Most appears in the lymph and is then widely distributed to all tissues. Most of a dose is slowly excreted in the bile and the remainder is eliminated in the urine as glucuronides of tocopheronicacid or other metabolites.

Niacinamide (Nicotinic Acid Amide)

Nicotinic acid is absorbed from the gastro-intestinal tract, is widely distributed in the body tissues and has a short half-life.

Calcium (Calcium Carbonate)

A third of ingested calcium is absorbed from the small intestine. Absorption of calcium decreases with age.

Calcium Pantothenate

Pantothenic acid is readily absorbed from the gastro-intestinal tract and is widely distributed in the body tissues. About 70%of pantothenic acid is excreted unchanged in the urine and about 30% in the faeces.

Folic Acid

Folic acid is absorbed mainly from the proximal part of the small intestine. Folate polyglutamates are considered to be deconjugated to monoglutamates during absorption. Folic acid rapidly appears in the blood where it is extensively bound to plasma proteins. Some folic acid is distributed in body tissues, some is excreted as folate in the urine and some is stored inthe liver as folate.

Vitamin B7 (Biotin)

Following absorption, biotin is stored in the liver, kidney and pancreas.

Selenium

Although it has been established that selenium is essential to human life, very little information is available on its functionand metabolism.

Copper Sulphate (Copper)

Copper is absorbed from the gastro-intestinal tract and its major route of excretion is in the bile.

Magnesium Sulphate (Magnesium)

Magnesium salts are poorly absorbed from the gastro-intestinal tract; however, sufficient magnesium will normally be absorbed to replace deficiency states. Magnesium is excreted in both the urine and the faeces but excretion is reduced indeficiency states.

Potassium Iodide (Potassium)

Potassium salts are absorbed from the gastro-intestinal tract. Potassium is excreted in the urine, the faeces and inperspiration. Urinary excretion of potassium continues even when intake is low.

Zinc Oxide (Zinc)

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

Manganese Oxide (Manganese)

Manganese salts are poorly absorbed.

Potassium Iodide (Iodine)

Iodides are absorbed and stored in the thyroid gland as thyroglobulin. Iodides are excreted in the urine with smalleramounts appearing in the faeces, saliva and sweat.

Chromium Chloride (Chromium)

Although it has been established that chromium is essential to human life, little information is available on its function andmetabolism.

Lycopene

Lycopene is absorbed in the small intestine after ingestion, along with dietary fat, at a rate of 7–10%. It's absorbed by passive diffusion across the intestinal cells' apical membrane, and possibly by a cholesterol membrane transporter called scavenger receptor class B type I (SR-BI). Other transporters may also help with absorption, but this hasn't been confirmed.

Valine, Leucine, Isoleucine

Valine, leucine, and isoleucine are all essential amino acids, also known as branched-chain amino acids (BCAAs). The small intestine absorbs these amino acids through a process that involves sodium cotransporters.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections ofthe SPC.

6. Pharmaceutical particulars

6.1 List of excipients

Zevit AM:

Excipients:
PVP K30
Isopropyl Alcohol
Talcum
Magnesium Stearate
Microcrystalline Cellulose
Sodium Starch Glycolate
Colloidal Silicon Dioxide

Coating:
Isopropyl Alcohol
Methylene Chloride
Insta Moistshield Coat-Purple

Zevit PM:

Excipients:
PVP K30
Isopropyl Alcohol
Talcum
Magnesium Stearate
Microcrystalline Cellulose
Sodium Starch Glycolate
Colloidal Silicon Dioxide

Lactose
Starch

Coating:
Isopropyl Alcohol
Methylene Chloride
Insta Moistshield Coat-Purple

6.2 Incompatibilities
None known

6.3 Shelf life
24 months

6.4 Special precautions for storage
Store in a cool dry place at temperature below 30 °C. Store in the original packaging.

6.5 Nature and contents of container
ALU – PVC pack in a printed carton

Pack size: Blister pack of 4 x 7 AM/PM.

7. Marketing authorization holder

Me Cure Industries PLC
Plot 6 Block H,
Debo Industries Compound,
Oshodi Industrial Scheme,
Oshodi, Lagos,
Nigeria.