

Product Information: MULTIREN TABLETS

Prescribing information (Summary of products characteristics):

1. Name of the Medicinal Product: MULTIREN TABLETS

2. Qualitative and Quantitative composition:

Each coated tablet contains Vitamin A (as acetate) BP 2500 IU, Vitamin D3 300 IU, Thiamine HCl BP 1 mg, Riboflavin BP 500 mcg, Ascorbic acid BP 15 mg, Nicotinamide BP 7.5 mg
For the full list of excipients, see section 6.1.

3. Pharmaceutical form: Oral Tablets

A green coloured round shaped biconvex sugar coated tablets, plain on both sides

4. Clinical particular's:

4.1 Therapeutic indication:

1. As a therapeutic nutritional adjunct where the intake of vitamins and minerals is suboptimal, e.g. in the presence of organic disease such as malignancy and immune deficiency syndromes, such as AIDS.
2. As a therapeutic nutritional adjunct in conditions where the absorption of vitamins and minerals is suboptimal, e.g. malabsorption, inflammatory bowel disease and fistulae, short bowel syndrome and Crohn's disease, and where concurrent medication decreases vitamin and mineral absorption.
3. As a therapeutic nutritional adjunct in convalescence from illness, e.g. where anorexia or cachexia exists and following chemo- or radio-therapy.
4. As a therapeutic nutritional adjunct in convalescence from surgery, e.g. where nutritional intake continues to be inadequate.
5. As a therapeutic nutritional adjunct for patients on special or restricted diets, e.g. in renal diets and where several food groups are restricted in therapeutic weight reducing diets.
6. As a therapeutic nutritional adjunct where food intolerance exists, e.g. exclusion diets.
7. As an adjunct in synthetic diets, e.g. in phenylketonuria, galactosaemia and ketogenic diets.

4.2 Posology and method of administration:

Adults and the Elderly

One tablet daily, preferably taken one hour after meals. Do not exceed the stated dose. The tablet should be swallowed whole with water.

Children under 12 years of age

Not recommended for this age group.

Method of administration

For oral administration.

4.3 Contraindication:

Hypercalcaemia, haemochromatosis and other iron storage disorders.
Hypersensitivity to the active substance(s) or to any of the excipients.

4.4 Special warning and precaution for use:

Whilst taking multivitamins both protein and energy are also required to provide complete nutrition in the daily diet. No other vitamins, minerals or supplements with or without vitamin A should be taken with this preparation except under medical supervision.

Do not take multivitamins on an empty stomach. Do not exceed the stated dose. Keep out of the reach of children. If symptoms persist, consult your doctor.

Important warning: Contains iron. Keep out of the reach and sight of children, as overdose may be fatal.

Evidence from Randomised Control Trials suggests that high doses (20-30 mg/day) b-carotene intake may increase the risk of lung cancer in current smokers and those previously exposed to asbestos. This high-risk population should consider the potential risks and benefits of multivitamins, which contain 4.5mg per recommended daily dose, before use.

Patients with thyroid disorders should seek medical advice before taking multivitamins. An allowance should be made for vitamins or minerals obtained from other sources.

4.5 Interactions with other medicinal products and other forms of interactions:

Folic acid can reduce the plasma concentration of phenytoin. Oral iron and zinc sulfate reduce the absorption of tetracyclines.

Additional information on special populations:

Not Applicable

Pediatric population:

Not Applicable

4.6 Fertility, pregnancy and lactation:

Multivitamins may be administered during pregnancy and lactation at the recommendation of the physician.

4.7 Effects on ability to drive and use machines:

None anticipated.

4.8 Undesirable effects:

Undesirable effects are listed by MedDRA System Organ Classes.

Assessment of undesirable effects is based on the following frequency groupings:

Very common: $\geq 1/10$

Common: $\geq 1/100$ to $< 1/10$

Uncommon: $\geq 1/1,000$ to $< 1/100$

Rare: $\geq 1/10,000$ to $< 1/1,000$

Very rare: $< 1/10,000$

Not known: cannot be estimated from the available data

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

4.9 Overdose and Treatment:

No cases of overdosage due to multivitamins therapy have been reported. Any symptoms which may be observed due to the ingestion of large quantities of multivitamins 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, lethargy and 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 coma and hepatocellular necrosis and renal failure.

Treatment

The following steps are recommended to minimise or prevent further absorption of the medication:

1. Administer an emetic.
2. Gastric lavage may be necessary to remove drug already released into the stomach. This should be undertaken using desferrioxamine solution (2 g/l). Desferrioxamine 5 g in 50 - 100 ml water should be introduced into the stomach following gastric emptying. Keep the patient under constant surveillance to detect possible aspiration of vomitus; maintain suction apparatus and standby emergency oxygen in case of need.
3. A drink of mannitol or sorbitol should be given to induce small bowel emptying.
4. Severe poisoning: in the presence of shock and/or coma with high serum iron levels (>142 µmol/l) immediate supportive measures plus i.v. infusion of desferrioxamine should be instituted. The recommended dose of desferrioxamine is 5 mg/kg/h by slow i.v. infusion up to a maximum of 80 mg/kg/24 hours. Warning: hypotension may occur if the infusion rate is too rapid.
5. Less severe poisoning: i.m. desferrioxamine 50 mg/kg up to a maximum dose of 4 g should be given.
6. Serum iron levels should be monitored throughout.
7. Any fluid or electrolyte imbalance should be corrected.

5. Pharmacological Properties:

5.1 Pharmacodynamic properties:

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 blindness which 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. Its involvement 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 B1 (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 effects on 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 and neurological symptoms. Gross deficiency of thiamine (and other Vitamin B group factors) leads to the condition beri-beri.

Vitamin B2 (Riboflavine)

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

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 electron donor 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. Features include 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.

Nicotinamide

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

5.2 Pharmacokinetic properties:

Vitamin A

Except when liver function is impaired, Vitamin A is readily absorbed. β -carotene (as in Forceval Capsules) 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 salts and 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 the blood. 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-intestinal tract into the circulation. In the liver, it is hydroxylated to 25-hydroxycholecalciferol, is subject to entero-hepatic circulation and is further hydroxylated to 1,25-dihydroxycholecalciferol in the renal tubule cells. Vitamin D metabolites are bound to specific plasma proteins.

Vitamin B1 (Thiamine)

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

Vitamin B2 (Riboflavine)

Riboflavine 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 riboflavine is converted to flavine mononucleotide (FMN) and then to flavine adenine dinucleotide (FAD).

Vitamin C (Ascorbic Acid)

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

Nicotinamide (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.

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 of the SPC.

6. Pharmaceutical Particulars:

6.1 List of excipients

Multiren contains the following excipients:

Maize starch, Dicalcium phosphate, Lactose, Sodium methyl paraben, Sodium propyl paraben, Microcrystalline cellulose, Magnesium stearate.

6.2 Incompatibilities

None known

6.3 Shelf life

24 Months

6.4 Special precaution for storage

Store in a cool, dry place below 30°C. Keep out of reach of children. Protect from light.

6.5 Nature and contents of container

10 tablets are packed in Aluminium /PVC foil blister strip and such ten blister strips are packed in a unit carton along with literature insert.

6.6 Special precautions for disposal

No special precaution

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURING SITE ADDRESSES:

Marketing Authorization Holder:

Rene Industries Ltd

Address: PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

Manufactured by:

Rene Industries Ltd

Address: PO Box 6034, Plot No.680, Kamuli, Kireka, Kampala, Uganda.

8. MARKETING AUTHORISATION NUMBER:

Not Applicable

9. DATE OF FIRST REGISTRATION/RENEWAL OF THE REGISTRATION:

Not Applicable

10. DATE OF REVISION OF THE TEXT:

Not Applicable

11. DOSIMETRY (IF APPLICABLE):

Not Applicable

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS (IF APPLICABLE):

Not Applicable