

## 1. Name of the medicinal product

Emvite Drops

## 2. Qualitative and quantitative composition

Emvite Drops contains 1333 IU retinol (as vitamin A palmitate), 400 IU ergocalciferol solution, 0.4 mg thiamine hydrochloride, 0.8 mg riboflavin, 0.8 mg pyridoxine hydrochloride, 8 mg nicotinamide, and 40 mg ascorbic acid in each 0.6 ml dose.

## 3. Pharmaceutical form

A yellow to orange brown oral drops solution which darkens upon storage, with some cloudiness.

## 4. Clinical particulars

### 4.1 Therapeutic indications

Emvite Drops is indicated for the prevention of vitamin deficiencies and for the maintenance of normal growth and health during the early years of infancy and childhood; multivitamin supplement.

### 4.2 Posology and method of administration

#### Adults and children over 12 years:

Not appropriate.

#### Children aged 1 to 12 years:

Oral. One 0.6 ml dose taken daily.

Maximum daily dose: 0.6 ml

#### Children under 1 year:

Oral. One 0.3 ml dose taken daily.

Maximum daily dose: 0.3 ml

#### The Elderly:

Not appropriate

#### Hepatic/renal dysfunction

Normal dosage is appropriate.

### 4.3 Contraindications

Emvite Drops is contraindicated in individuals with known hypersensitivity to the product or any of its components including peanut oil.

Emvite Drops contains Arachis oil (peanut oil) and should not be taken by patients known to be allergic to peanut. As there is a possible relationship between allergy to peanut and allergy to Soya, patients with Soya allergy should also avoid Emvite Drops.

### 4.4 Special warnings and precautions for use

When prescribing Emvite Drops, as with all multi-vitamin preparations, allowance should be made for vitamins obtained from other sources.

While children are taking Emvite Drops no other vitamin supplement containing vitamins A and D should be taken unless under medical supervision.

This multivitamin supplement should not be given to babies who are receiving more than 500mls of formula milk per day to avoid exceeding the safe upper limit of Vitamin A.

Excessive dosage of vitamin A and D may lead to hypervitaminoses. Due allowance should always be made for intake of these vitamins from other sources.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

#### **4.5 Interaction with other medicinal products and other forms of interaction**

None.

#### **4.6 Pregnancy and lactation**

Not indicated.

#### **4.7 Effects on ability to drive and use machines**

None known

#### **4.8 Undesirable effects**

##### **Vitamin A palmitate**

Adverse effects are extremely rare at daily doses of less than 9 mg (16363.6 iu).

##### **Ergocalciferol (Vitamin D<sub>2</sub>)**

The only known adverse effects of vitamin D occur when excessive doses are taken. Adverse effects are not anticipated at the quantity present in Emvite Drops.

##### **Ascorbic Acid (C), Nicotinamide, Pyridoxine (B<sub>6</sub>), Riboflavin (B<sub>2</sub>) & Thiamine (B<sub>1</sub>)**

These water soluble vitamins are generally non toxic compounds with a wide margin of safety, the excess amounts being rapidly excreted in the urine. Adverse effects are not anticipated at the quantities present in Emvite Drops.

#### **4.9 Overdose**

##### **Symptoms and signs**

Emvite Drops contains levels of vitamins which present little risk in overdose.

##### **Vitamin A palmitate**

Acute administration of high doses of vitamin A can cause headache, nausea, vomiting and irritability. In infants acute toxicity can lead to transient hydrocephalus. All these effects disappear within 24 hours of taking retinol.

##### **Ergocalciferol (Vitamin D<sub>2</sub>)**

Excessive doses of vitamin D, 60 000 units per day, can result in hypercalcaemia and hypercalciuria. Adverse effects of hypercalcaemia may include muscle weakness, apathy, headache, anorexia, nausea and vomiting, hypertension and cardiac arrhythmias.

##### **Thiamine hydrochloride (Vitamin B<sub>1</sub>)**

When taken orally, thiamine is non-toxic. If large doses are ingested they are not stored by the body but excreted unchanged by the kidneys.

##### **Riboflavin (Vitamin B<sub>2</sub>)**

Riboflavin has been found to be practically non-toxic.

##### **Pyridoxine hydrochloride (Vitamin B<sub>6</sub>)**

Acute doses less than 500mg per day appear to be safe. Excessive doses may lower serum folate concentrations. Sensory neuropathy has been described with chronic dosing of 200 mg daily.

##### **Nicotinamide**

A single large overdose of nicotinamide is unlikely to have serious ill effects, though transient abnormalities of liver function might occur.

##### **Ascorbic acid (Vitamin C)**

Ascorbic acid is not stored to a great extent by the body, any excess amounts are eliminated in the urine. Ascorbic acid is thought to become toxic at chronic doses in excess of 6 g.

## Treatment

Treatment should be supportive and symptomatic.

## 5. Pharmacological properties

### 5.1 Pharmacodynamic properties

#### Vitamin A palmitate

Vitamin A plays an essential role in the function of the retina, the growth and function of epithelial tissue, bone growth, reproduction and embryonic development.

#### Ergocalciferol (Vitamin D<sub>2</sub>)

Vitamin D is a regulator of both calcium and phosphate homeostasis.

#### Thiamine hydrochloride (Vitamin B<sub>1</sub>)

Vitamin B<sub>1</sub> is essential for proper carbohydrate metabolism and plays an essential role in the decarboxylation of alpha keto acids.

#### Riboflavin (Vitamin B<sub>2</sub>)

Riboflavin is essential for the utilisation of energy from food. It is a component of co-enzymes which play an essential role in oxidative/ reductive metabolic reactions. Riboflavin is also necessary for the functioning of pyridoxine and nicotinic acid.

#### Pyridoxine hydrochloride (Vitamin B<sub>6</sub>)

Vitamin B<sub>6</sub> is a constituent of the co-enzymes, pyridoxal pyrophosphate and pyridoxamine phosphate, both of which play an important role in protein metabolism.

#### Nicotinamide

Nicotinamide is an essential component of co-enzymes responsible for proper tissue respiration.

#### Ascorbic acid (Vitamin C)

Ascorbic acid is a water soluble vitamin and a powerful antioxidant.

It is a cofactor in numerous biological processes, such as the metabolism of folic acid, amino acid oxidation and the absorption and transport of iron.

It is also required for the formation, maintenance and repair of intercellular cement material. Ascorbic acid is important in the defence against infection, the normal functioning of T-lymphocytes and for the effective phagocytic activity of leucocytes. It also protects cells against oxidation damage to essential molecules.

### 5.2 Pharmacokinetic properties

#### Absorption

Vitamins A, B<sub>1</sub>, B<sub>2</sub>, B<sub>6</sub>, C, D<sub>2</sub> and nicotinamide are well absorbed from the gastro-intestinal tract.

#### Distribution

The vitamins present in Emvite Drops are widely distributed to all tissues in the body.

#### Metabolism and elimination

#### Vitamin A palmitate

Vitamin A palmitate is hydrolysed in the intestinal lumen to retinol which is then absorbed. Retinol circulates in the blood bound to retinol binding protein which protects it from glomerular filtration. The complex circulates to target tissues where the vitamin is released, permeates the cell and binds intracellularly to cellular retinol binding protein. Of the absorbed retinol 20 - 50 % is either conjugated or oxidised to various products and excreted over a matter of days in the urine and faeces, while the remainder is stored. This stored retinol is gradually metabolised by the liver and peripheral tissues.

**Ergocalciferol (Vitamin D<sub>2</sub>)**

Vitamin D circulates in the blood associated with vitamin D binding protein. It is stored in fat deposits. Ergocalciferol is hydroxylated in the liver and gut to 25-hydroxy colecalciferol which is then further metabolised in the kidney to the active form 1,25-dihydroxycolecalciferol and other hydroxylated metabolites. Ergocalciferol and its metabolites are excreted largely in bile with eventual elimination in the faeces, with only small amounts of some of the metabolites appearing in the urine.

**Thiamine hydrochloride (Vitamin B<sub>1</sub>)**

Thiamine has a plasma half life of 24 hours and is not stored to any great extent in the body. Excess ingested thiamine is excreted in the urine as either the free vitamin or as the metabolite, pyrimidine.

**Riboflavin (Vitamin B<sub>2</sub>)**

Following absorption riboflavin is converted into the co-enzymes: flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD).

Riboflavin is not stored in body tissues to any great extent and amounts in excess of the body's requirements are excreted in the urine largely unchanged.

**Pyridoxine hydrochloride (Vitamin B<sub>6</sub>)**

The half life of pyridoxine ranges from 15 - 20 days. Once absorbed vitamin B6 is converted to its active co-enzyme form pyridoxal 5-phosphate. Muscle is the major storage site for pyridoxal 5-phosphate. It is degraded in the liver to 4-pyridoxic acid which is eliminated by the kidneys.

**Nicotinamide**

Nicotinamide is readily taken up into tissues and utilised for the synthesis of the co-enzyme forms nicotinamide adenine dinucleotide (NAD) and nicotinamide adenine dinucleotide phosphate (NADP). Nicotinamide is degraded in the liver and other organs to a number of products that are excreted in the urine, the major metabolites being n-methyl-2-pyridone-5-carboxamide and n-methylnicotinamide.

**Ascorbic acid (Vitamin C)**

Ascorbic acid reaches a maximum plasma concentration 4 hours following oral administration after which there is rapid urinary excretion. Following oral administration 60 % of the dose is excreted in 24 hours either as ascorbic acid or its metabolite dihydroascorbic acid.

**Pharmacokinetics in Renal Impairment**

There have been no specific studies of Emvite Drops in renal impairment.

**Pharmacokinetics in the Elderly**

Not appropriate.

**5.3 Preclinical safety data****Mutagenicity**

There is insufficient information to determine the mutagenic potential of the active ingredients. However very large doses of vitamin C are claimed to be mutagenic.

**Carcinogenicity**

There is insufficient information to determine the carcinogenic potential of the active ingredients.

**Teratogenicity**

High doses of vitamin D are known to be teratogenic in experimental animals, but direct evidence for this is lacking in humans.

The teratogenicity of vitamin A in animals is well known, both high and low levels of the vitamin result in defects. But the significance of this for humans is in dispute. Synthetic versions of vitamin A (Isotretinoin and Etretinate) have been shown to be powerful teratogens. There is insufficient information to determine the teratogenic potential of the other active ingredients.

**Fertility**

Not appropriate.

**6. Pharmaceutical particulars****6.1 List of excipients**

Sodium hydroxide

Sugar (mineral water grade)

Refined peanut oil (a carrier for Vitamin A palmitate)

Polysorbate 60

Purified water

Nitrogen, Oxygen free

**6.2 Incompatibilities**

None known.

**6.3 Shelf life**

18 months after manufacture.

Once opened use within 4 weeks.

**6.4 Special precautions for storage**

Do not store above 25°C. Keep bottle in the outer carton.

**6.5 Nature and contents of container**

Emvite Drops are presented in an amber Type III glass bottle, with Tamper-evident Polypropylene cap or ROPP aluminium cap containing a PET/ Aluminium/ Polyethylene/ Expanded Polyethylene laminated wad.

One or two 25 ml bottles are enclosed in a printed cardboard carton with one polyethylene / polystyrene syringe graduated at 0.3 ml and 0.6 ml. Alternatively, two cartons containing a 25 ml bottle and polyethylene / polystyrene syringe may be shrink wrapped to provide a pack size of 50 ml.

**6.6 Special precautions for disposal and other handling**

None applicable.

**7. Marketing authorisation holder**

Emzor Pharmaceutical Industries Limited

Plot 3C,Block A,Aswani Market Road,Isolo-Lagos,Nigeria

**8. Marketing authorisation number(s)**

NA

**9. Date of first authorisation/renewal of the authorisation**

NA

**10. Date of revision of the text**

NA