

1. NAME OF THE MEDICINAL PRODUCT

Novavite Multivitamin Drops

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 0.6ml contains Vitamin A 4,000I.U, Vitamin B1 1mg, Vitamin B2 0.4mg, Vitamin B6 0.5mg, Vitamin C 25mg, Vitamin D2 400 I.U Nicotinamide 5mg. For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM

Novavite Drops is presented as a yellow to orange brown oral drops solution which darkens upon storage, with some cloudiness.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Novavite Multivitamin 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

Posology

Route: Oral administration.

Adults and children over 12 years: Not appropriate.

Babies aged 0 to 12 months: One 0.3 ml dose taken daily.

Infants over 12 months: One 0.6 ml dose taken daily.

The Elderly: Not appropriate

Hepatic/renal dysfunction

Normal dosage is appropriate.

Method of administration

Novavite Drops should be given as a single daily dose dropped at the back of the tongue or mixed with milk, cereal, fruit juice or other fluids.

4.3 Contraindications

Novavite Multivitamin Drops is contraindicated in;

- Individuals with known hypersensitivity to the product or any of its components.
- Concurrent administration of other vitamin A or vitamin D-containing products

4.4 Special warnings and precautions for use

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

While children are taking Novavite Multivitamin 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 D₂)

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

Ascorbic Acid (C), Nicotinamide, Pyridoxine (B₆), Riboflavin (B₂) & Thiamine (B₁)

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 Novavite Multivitamin Drops.

4.9 Overdose

Symptoms and signs

Novavite Multivitamin 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 D₂)

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 B₁)

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 B₂)

Riboflavin has been found to be practically non-toxic.

Pyridoxine hydrochloride (Vitamin B₆)

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 D₂)

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

Thiamine hydrochloride (Vitamin B₁)

Vitamin B₁ is essential for proper carbohydrate metabolism and plays an essential role in the decarboxylation of alpha keto acids.

Riboflavin (Vitamin B₂)

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 B₆)

Vitamin B₆ 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 defense 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, B₁, B₂, B₆, C, D₂ and nicotinamide are well absorbed from the gastro-intestinal tract.

Distribution

The vitamins present in Novavite Multivitamin 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 D₂)

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 B₁)

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 B₂)

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 B₆)

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 Novavite Multivitamin 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**

Vitamin A + Vitamin D (Water Miscible), Ascorbic Acid, Nicotinamide, Thiamine Hydrochloride, Riboflavine-5-Monosodium Phosphate, Pyridoxine Hydrochloride, Methyl Hydroxybenzoate, Liquid Glucose, Polysorbate 80, Glycerol, Sorbitol Solution 70%, Purified Water.

6.2 Incompatibilities

None known.

6.3 Shelf life

2 years

6.4 Special precautions for storage

Product should be stored below 30°C and protected from light.

6.5 Nature and contents of container

Novavite Multivitamin Drops is presented in 15ml amber Type III glass bottle, with 22mm ROPP aluminium cap containing a latex wad.

One 15ml bottle is enclosed in a printed cardboard carton with one 1ml polyethylene/ polystyrene calibrated dropper.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER

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