N-XAMINE® SYRUP

(MULTIVITAMIN, MINERALS, ANTI-OXIDANT SYRUP)

SUBMITTED BY: NALIS PHARMACEUTICALS LTD

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SUMMARY OF PRODUCT CHARACTERISTICS

(SmPC).

1 NAME OF THE MEDICINAL PRODUCT:

N-Xamine Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Red-coloured syrup
Each 5 ml contains:
Lycopene……**...4000 mcg**
Copper cupric iodide)……**500 mcg**
Folic acid……**400 mcg**
Vitamin C……**100 mg**
Iodine as Potassium iodide….**20 mcg**
Manganese chloride……2 **mcg**
Mecobalamin……2 **mcg**
Nicotinamide……**.10 mcg**
Vitamin E……2000 **mcg**
Vitamin A……**.1000 mcg**
Vitamin B1……1000 **mcg**
Vitamin B6 ……1000 **mcg**
Zinc sulphate……2000 **mcg**
Excipients……**qs**

3. PHARMACEUTICAL FORM

Oral Syrup

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

N-Xamine Syrup contains multivitamins and minerals which are used to provide substances that are not taken in through the diet. Multivitamins and minerals are also used to treat vitamin or mineral deficiencies caused by illness, pregnancy, poor nutrition, digestive disorders, certain medications, and many other conditions.

4.2 Posology and method of administration

For oral administration.

Adults
In the average case therapy is started with 10ml three times a day'
Prpphylactic dose should be 5ml once or twice a day.

Elderly
The dose is the same as adult dose

Paediatric population
The dose for children is 5ml once or twice a day or as directed by the physician

4.3 Contraindications

N-Xamine is contraindicated in the following conditions:

- **a high amount of oxalic acid in urine**
- **iron metabolism disorder causing increased iron storage**
- **sickle cell anemia**
- **anemia from pyruvate kinase and G6PD deficiencies**
- **Patients with hypersensitivity to this class of drugs. It should be prescribed with caution to patients with hepatic disease, renal disease, alcoholism, and acne vulgaris.**
- **decreased blood-clotting from low vitamin K**
- **increased risk of bleeding due to clotting disorder**

4.4 Special warnings and precautions for use

Do not take this drug if you are allergic to multivitamins or any ingredients contained in this drug.
Keep out of reach of children. In case of overdose, get medical help.

4.5 Interaction with other medicinal products

- **Many drugs are known to interact with multivitamins and minerals. The interactions are classified into**
- **major drug interactions**
- **moderate drug interactions**
- **minor drug interaction. Consult your physician or Pharmacist before combining multivitamins with other drugs.**

4.6 Pregnancy and lactation

Pregnancy
The IOM recommends multivitamins that contain iron, zinc, copper, calcium, folic acid, and vitamins D, C, B6, and B12 (note that iodine is not included) for some groups of pregnant women, such as those with iron-deficiency anemia or poor-quality diets, vegetarians, cigarette smokers, and those who consume alcohol.
Folic acid is a B vitamin that every cell in your body needs for healthy growth and development. Taking folic acid before and during early pregnancy can help prevent birth defects of the brain and spine called neural tube defects

Breastfeeding

- **Most mineral supplements (e.g., iron, calcium, copper, chromium, zinc) taken by the mother do not affect breastmilk levels.**
- **Water soluble vitamin supplements (e.g., B vitamins, vitamin C) taken by the mother usually increase breastmilk levels. Breastmilk levels of some water-soluble vitamins, such as vitamin C, only increase up to a certain point, then remain steady – even if mom increases her dose.**
- **Fat soluble vitamin supplements (e.g., vitamins A & E) taken by the mother can concentrate in human milk, and thus excessive amounts may be harmful to a breastfeeding baby.**

Fertility
Folic acid is an important vitamin, not only for women trying to conceive, but during the first three months of pregnancy. Folic acid can help increase your chances of becoming pregnant and is an important nutrient in helping the baby's spine develop the w**ay it should**
Studies have shown that folic acid also has fertility benefits for men, increasing the quality and quantity of sperm.
Research shows that giving women vitamin B6 can increase their chances of becoming pregnant
Researches have shown that regular use of multivitamin supplements may decrease the risk of ovulatory infertility.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

When taken as directed, multivitamins are not expected to cause serious side effects. Common side effects may include:

- upset stomach;
- headache; or
- unusual or unpleasant taste in your mouth.

This is not a complete list of side effects and others may occur.

4.9 Overdose

Overdose symptoms may include stomach pain, vomiting, diarrhea, constipation, loss of appetite, hair loss, peeling skin, tingly feeling in or around your mouth, changes in menstrual periods, weight loss, severe headache, muscle or joint pain, severe back pain, blood in your urine, pale skin, and easy bruising or bleeding.

If overdose is suspected, your doctor should be contacted immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Multivitamins and Minerals
ATC Code: A11AA

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.

Vitamin B_1 is essential for proper carbohydrate metabolism and plays an essential role in the decarboxylation of alpha keto acids.

Riboflavin is essential for the utilization 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.

Vitamin B_6 is a constituent of the co-enzymes, pyridoxal pyrophosphate and pyridoxamine phosphate, both of which play an important role in protein metabolism.

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

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.

Lycopene is a powerful antioxidant with many health benefits, including sun protection, improved heart health and a lower risk of certain types of cancer. Though it can be found as a supplement, it may be most effective when consumed from lycopene-rich foods like tomatoes and other red or pink fruits

Mechanism of action
Vitamins and minerals are considered essential nutrients—because acting in concert, they perform hundreds of roles in the body. They help shore up bones, heal wounds, and bolster your immune system. They also convert food into energy, and repair cellular damage.

Vitamin B9(folic acid)is a precursor needed to make, repair, and methylate DNA; a cofactor in various reactions; especially important in aiding rapid cell division and growth, such as in infancy and pregnancy.

Vitamin B6 is coenzyme in many enzymatic reactions in metabolism.

Nicotinamide is a precursor of coenzymes called NAD and NADP, which are needed in many metabolic processes.

Riboflavin is a precursor of cofactors called FAD and FMN, which are needed for flavoprotein enzyme reactions, including activation of other vitamins.

Vitamin B1 is a coenzyme in the catabolism of sugars and amino acids.

Zinc is component of many metalloenzymes. Example: Red blood cell carbonic anhydrase, Alkaline phosphatase, alcohol dehydrogenase, carboxy-peptidase, SOD (cytosol) • Many enzymes involved in RNA and DNA synthesis, such as DNA and RNA polymerases. Iron combines with porphyrin and globin chains to form hemoglobin, which is critical for oxygen delivery from the lungs to other tissues.

Lycopene functions as a very potent antioxidant, and this is clearly a major important mechanism of lycopene action. In this regard, lycopene can trap singlet oxygen and reduce mutagenesis in the Ames test. However, evidence is accumulating for other mechanisms as well. Lycopene at physiological concentrations can inhibit human cancer cell growth by interfering with growth factor receptor signaling and cell cycle progression specifically in prostate cancer cells without evidence of toxic effects or apoptosis of cells. Studies using human and animal cells have identified a gene, connexin 43, whose expression is upregulated by lycopene and which allows direct intercellular gap junctional communication (GJC).

5.2 Pharmacokinetic properties

Absorption

Vitamin B_{12} substances bind to intrinsic factor; glycoproteins secreted by the gastric mucosa and are then actively absorbed from the gastrointestinal tract. Absorption is impaired in patients with an absence of intrinsic factor.
Absorption of lycopene requires that it be combined with bile salts and fat to form micelles. Intestinal absorption of lycopene is enhanced by the presence of fat and by cooking. Lycopene dietary supplements (in oil) may be more efficiently absorbed than lycopene from food.
Pyridoxine B6 (pyridoxal and pyridoxamine) are readily absorbed from the gastrointestinal tract after oral doses and are converted to the active forms: pyridoxal phosphate and pyridoxamine phosphate.
Riboflavin is readily absorbed from the gastrointestinal tract. Although riboflavin is widely distributed to body tissues little is stored in the body. Small amounts of thiamine are well absorbed from the gastrointestinal tract after oral doses, but the absorption of doses larger than about 5mg is limited.
Absorption of zinc from the gastrointestinal tract is incomplete and is reduced in the presence of some dietary constituents such as phytates. Bioavailability of dietary zinc varies widely between different sources, but is about 20 to 30%.Folic acid given therapeutically enters the portal circulation largely unchanged, since it is a poor substrate for reduction by dihydrofolate reductase. It is converted to the metabolically active form 5 methltetrahydrofolate in the plasma and liver.Iron is irregularly and incompletely absorbed from the gastrointestinal tract, the main sites of absorption being the duodenum and jejunum. Absorption is aided by the acid secretion of the stomach and by some dietary acids (such as ascorbic acid) and occurs more readily when the iron is in the ferrous state or is part of the haem complex (haem-iron). Absorption is also increased in conditions of iron deficiency or in the fasting state but is decreased if the body stores are overloaded. Normally only about 5 to 15% of the iron ingested in food is absorbed.

Distribution

Vitamin B_{12} is stored in the liver, excreted in the bile and most of it in the first 8 hours; urinary excretion, however, accounts for only a small fraction in the reduction of total body stores acquired by dietary means. Vitamin B_{12} diffuses across the placenta and also appears in breast milk.
Pyridoxine is stored mainly in the liver where there is oxidation to 4-pyridoxic acid.Pyridoxal crosses the placenta and is distributed into breast milk.Riboflavine also crosses the placenta and is distributed into breast milk.It is widely distributed to most body tissues and appears in breast milk. Thiamine is not stored to any appreciable extent in the body and amounts in excess of the body's requirements are excreted in the urine unchanged or as metabolites.. Zinc is distributed throughout the body with the highest concentrations found in muscle, bone, skin, eye and prostatic fluids.The principal storage site of folate is the liver; it is also actively concentrated in the Cerebrospinal fluid. Folate undergoes enterohepatic circulation .. Folate is distributed into breast milk. Folic acid is removed haemodialysis.Most absorbed iron is bound to transferrin and transported to the bone marrow where it is incorporated into haemoglobin; the remainder is contained within the storage forms, ferrtin or haemodiderin, or as myoglobin with smaller amounts occurring in haemcontaining enzymes or in plasma bound to transferring.

Elimination

Lycopene was extensively isomerized after dosing and rapidly metabolized into polar metabolites excreted into urine with the rapid peak of $^{14}CO_2$ after dosing, which implies that β-oxidation was involved in the lycopene metabolism. Lycopene or its metabolites were detected in skin.
Vitamin B12 undergoes extensive enterohepatic recycling; part of a dose is excreted in the urine.
Pyridoxine. As the dose increases, proportionally greater amounts are excreted unchanged in the urine.

Riboflavin is excreted in urine, partly as metabolites.Zinc is primarily excreted in the faeces and regulation of faecal losses is important in zinc homoeostasis. Small amounts are lost in urine and perspiration. Folate metabolites are eliminated in the urine and folate in excess of body requirements is excreted unchanged in the urine.

5.3 Preclinical safety data

None.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium CMC, Ethanol, Propylene Glycol, Methyl Paraben, Propyl Paraben, Glycerine, Tween 80, Xanthan Gum, Sugar, Strawberry Flavour, Carmoisine Red, Sodium Benzoate, Treated Water

6.2 Incompatibilities

None stated except as in 'Interactions with other medicaments'.

6.3 Shelf life

36 months

6.4 Special precautions for storage

Do not store above 30°C.
Keep away from light

6.5 Nature and contents of container

200 ml Pet bottles with ROPP caps and measuring device (dispensing cups).

6.6 Special precautions for disposal and other handling

None

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

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9. NAFDAC REGISTRATION NUMBER(S)

A11-100054