SUMMARY OF PRODUCT CHARACTERISTICS

(a) Name of Product

Proprietary :**CODATEMIN (TONIC)**

Generic : (IRON &MULTIVITAMIN)

(b) Promotional Category

Prescription Only Medicine (POM)

Dosage form

LIQUID DOSAGE FORM (SYRUP)

Route and Conditions of Administration

Route: Oral

Name and Quantity of Each Ingredient:

Indication (s):

Treatment of pernicious anemia and other vitamin B deficiency state. It is a vitamin and iron supplement.

S/N	INGREDEINTS	QTY/5Ml
1.	Ferric ammonium citrate	80mg
2.	Vitamin B12 (Cyanocobalamine	5mcg
3.	Vitamin B9 (Folic Acid)	0.5mg
4.	Xanthan gum	12.5mg
5.	Sodium benzoate	10mg
10	Sorbitol 70%	25mg
11.	Saccharine sodium	2.5mg
12.	Raspberry flavour	5mg
13.	Mixed fruits flavour	5mg
14.	Caramel colour	25mg
15.	Methyl Paraben	10mg
16.	Propyl Paraben	1mg
17.	Sugar	875mg
18.	Citric Acid	6.25mg
19.	Sodium hydroxide	0.175mg

CLINICAL DATA

Vitamin B complex typically consists of the water-soluble vitamins biotin, folic acid, thiamin, riboflavin, niacin, pantothenic acid, pyridoxine, and the cobalamins (vitamin B12).1 Choline, para-aminobenzoic acid, and inositol are also found in some B complex supplement products.1 Thiamin, riboflavin, niacin, vitamin B6, pantothenic acid, and biotin are necessary for energy metabolism at rest and during physical activity; folate and vitamin B12 are essential for red blood cell production, tissue repair, and protein synthesis.2 Vitamin B complex purportedly has enhancing effects on energy metabolism, cell regeneration, and cognitive function.3,4 An adequate intake of B vitamins is essential to maintain health and optimum exercise performance.2 Low levels of B vitamins may result in decreased physical ability, particularly during high-intensity situations.4 Dose Range and Upper Limit Food and Nutrition Board DRIs5 RDA/AI & Upper Limit: RDA/AI Men 19-50 RDA/AI Women 19-50 Upper Limit (UL) B Vitamin B1 – Thiamin (mg) 1.2 1.1 Not established B2 – Riboflavin (mg) 1.3 1.1 Not established B3 – Niacin (mg) 16 14 35 B5 – Pantothenic acid (mg) 5* 5* Not established B6 – Pyridoxine (mg) 1.3 1.3 100 B7 – Biotin (mcg) 30* 30* Not established B9 – Folic acid (mcg) 400 400 1000 B12 – Cobalamin (mcg) 2.4 2.4 Not established *RDA not established; Adequate Intake (AI) provided Doses Used in Randomized Clinical Trials: No data were found for combinations of B vitamins for enhancing performance. Toxicology Data: No data were found for combinations of B vitamins. The following have been reported for specific B vitamins: B1/Thiamin. No data found; generally recognized as nontoxic.1 B2/Riboflavin. Doses of 400 mg per day may cause diarrhea and polyuria (excessive urine production).1 B3/Niacin. For doses larger than three grams per day, side effects may include liver problems, gout, digestive tract ulcers, loss of vision, high blood sugar, irregular heartbeat, and other problems.1 B5/Pantothenic acid. Consumption up to 10 grams has not shown adverse effects. Large amounts can cause diarrhea

B6/Pyridoxine. The tolerable upper intake level is 100 mg/day for adults. Doses greater than 1000 mg daily pose a risk for sensory neuropathy (nerve damage).1 B7/Biotin. No data found; doses of 10 mg per day did not produce adverse effects.1 B9/Folic acid. The tolerable upper intake level is 1000 mcg for adults. Some research suggests that doses of 800-1200 mcg daily for 3-10 years may increase the risk of cancer and heart attack in people who have existing heart problems.1 B12/Cobalamin. No data found. Evaluation of Potential Benefits There is no scientific evidence that supplementing with vitamin B complex improves energy metabolism or cognitive function. Based on controlled studies, the current requirements for increasing the B vitamin content of combat rations could enhance physical and mental performance of soldiers.6 Currently the MRE contains more than two times the Nutritional Standards for Operational Rations (NSOR) for B vitamins. Potential Detrimental Effects on… Military Performance: Severe folate and vitamin B12 deficiencies could result in anemia and decreased physical performance.7 Military Survivability: No data found. Other Health Risks No data found for vitamin B complex. At certain doses and for some people, high doses of riboflavin, pantothenic acid, and vitamin B12 can cause diarrhea.1 Depending on the form and dose, vitamin B6

supplementation can cause nausea, vomiting, headache, and loss of appetite.1 Interactions with Medications or Other Bioactive Substances B1/Thiamin. No known drug interactions. Chewing of bêtel nuts may cause thiamin deficiency. For those at risk of thiamin deficiency, avoid the use of the herb horsetail (equisetum).1 B2/Riboflavin. Anxiolytics (Phenobarbital) – minor interaction.1 In healthy women, psyllium reduces riboflavin absorption from supplements.1 B3/Niacin. NSAIDs (aspirin) – minor interaction.1 Taking niacin and chromium together may lower blood sugar. Taking niacin with androstenedione, borage leaf, chaparral, comfrey, DHEA, germander, kava, pennyroyal oil, or red yeast can increase the risk of liver damage, especially with higher doses of niacin. Taking zinc and niacin together may increase the risk of niacin side effects such as flushing and itching.1 B5/Pantothenic acid. No known drug interactions. Note that royal jelly contains pantothenic acid; the effects of taking them together are not known.1 B6/Pyridoxine. Anxiolytics (Phenobarbital) – moderate interaction.1 B7/Biotin. No known interactions. B9/Folic acid. Anxiolytics (Phenobarbital) – moderate interaction.1 Green tea may decrease folic acid activity.1 B12/Cobalamin. No known drug interactions. Large doses of folic acid can mask vitamin B12 deficiency. For some, potassium supplements may decrease the absorption of vitamin B12.1

Physiologic roles and deficiency signs of B-complex vitamins

Vitamin	Physiologic roles	Deficiency
Thiamin (B_1)	Co-enzyme functions in metabolism of carbohydrates and branched-chain amino acids	Beri-beri, polyneuritis, and Wernicke-Korsakoff syndrome
Riboflavin (B_2)	Co-enzyme functions in numerous oxidation and reduction reactions	Growth, cheilosis, angular stomatitis, and dermatitis
Niacin (nicotinic acid and nicotinamide)	Co-substrate/co-enzyme for hydrogen transfer with numerous dehydrogenases	Pellagra with diarrhoea, dermatitis, and dementia
Vitamin B_6 (pyridoxine, pyridoxamine, and pyridoxal)	Co-enzyme functions in metabolism of amino acids, glycogen, and sphingoid bases	Naso-lateral seborrhoea, glossitis, and peripheral neuropathy (epileptiform convulsions in infants)
Pantothenic acid	Constituent of co-enzyme A and phosphopantetheine involved in fatty acid metabolism	Fatigue, sleep disturbances, impaired coordination, and nausea
Biotin	Co-enzyme functions in bicarbonate-dependent carboxylations	Fatigue, depression, nausea, dermatitis, and muscular pains

Bioavailability / Bioequivalence:

Definitions: bioavailability and bioequivalence

The concept of vitamin and mineral bioavailability for dietary supplements lacks standard scientific and regulatory definitions. Commonly used definitions include concepts of absorption (27) and some also include utilization (eg, availability for use or storage) (28-30). For some nutrients, beneficial functions of unabsorbed nutrients (eg, binding of bile salts by calcium in the gut) would be missed by absorption-based definitions . Similar to the situation for drugs, definitions of nutrient bioavailability may benefit from a provision for functionality at sites of action not dependent on systemic blood circulation for delivery of the active moiety .

Bioequivalence is closely related to the concept of bioavailability . For some nutrients, equal absorption does not mean equal biological effects because the nutrient sources are chemically different, resulting in differences in nutrient activity . Bioavailability and bioequivalence factors are the basis for adjustments for some nutrient reference values . For example, differences in the activity of different chemical sources of vitamin A and folate are converted to vitamin equivalents when setting Recommended Dietary Allowances (RDAs). The effect on intake estimates for folate equivalents versus micrograms is illustrated . For other nutrients (eg, iron, niacin, vitamin B-6, and vitamin B-12), RDA or Adequate Intake (AI) values are adjusted on the basis of different bioavailabilities and bioequivalencies from mixed diets, making their use for dietary supplements problematic.

DRUG INTERACTIONS

Drug-nutrient interactions are the result of both host and nutrient-drug factors. These interactions can make a drug less effective, increase the action of a drug, or cause unexpected side effects. There are also reports of certain drugs decreasing the effectiveness of vitamins and minerals. Little research-based information is available on potential or actual drug-vitamin or drug-mineral interactions. Reported interactions include vitamin E and aspirin with the potential for an additive antithrombotic effect and between vitamin E and warfarin related to an increased risk of bleeding (55). An antioxidant supplement containing vitamins C and E, β-carotene, and selenium used in the treatment arm of a randomized controlled clinical trial blocked the beneficial response of HDL to simvastatin-niacin therapy in patients with coronary artery disease and low HDL (56). The vitamin-drug and mineral-drug interactions that have been reported in the Thomson **Micromedex Healthcare Series**

Dietary supplement manufacturers have not been required to evaluate the potential for drug interactions, but legislation to mandate the reporting of serious adverse effects is currently under consideration. Reports of suspected or documented adverse events may be voluntarily submitted to the Food and Drug Administration's MedWatch program (58) or other organizations, such as poison control centers. If drug-MVM supplement interactions are documented, information identifying this would more likely be required for drug labeling than for supplement labeling. However, manufacturers and retailers may voluntarily place warning statements on MVMs. These statements do not require review or approval by the Food and Drug Administration.

Toxicological Data

- **Vitamin B1**
- Vitamin B1 toxicity is very rare and this is one of the safest of the vitamins. However, excessive vitamin B1 can deplete other B vitamins and disrupt insulin and thyroid production.
- **Vitamin B2**
- You may notice a yellow coloration of the urine when you take supplements of vitamin B2. This is completely normal.
- **Vitamin B3**
- Those suffering from diabetes, glaucoma, gout, liver disease, or peptic ulcers should use niacin supplements cautiously. Consuming over 500 mg per day for an extended length of time may result in liver damage.
- High doses of nicotinic acid and nicotinamide can alter liver function tests, changes which quickly reverse when treatment is stopped or the dosage reduced.
- Niacin can cause a somewhat irritating but harmless flushing when first taking a dose of 50 milligrams or more. A no-flush variety, inositol hexanicotinate is the only form of time release niacin that is recommended; other forms of time-release niacin are a liver irritant and should not be consumed. The niacin flush may be worse when also taking antibiotics.
- Some studies indicate that doses higher than 500 mg may cause some liver damage.
- **Vitamin B5**
- This is one of the safest vitamins. It has no known side effects or toxic levels.
- **Vitamin B6**
- Vitamin B6 should not be taken by anyone undergoing levodopa treatment for Parkinson's disease.
- Excess vitamin B6 can deplete other B vitamins, so always take it in balanced amounts. Therapeutic dosages should not be used long-term unless they are under a total of 100 - 200 mg daily (except with the supervision of a physician).
- If taking doses larger than 50 mg for therapeutic benefit, the doses should be divided into 50 mg doses, which can be taken during the course of the day. This is important because the liver is unable to handle more than a 50 mg dose at a time.
- **Vitamin B12**
- There are no reported cases of vitamin B12 toxicity and it appears to be safe at any dosage level.
- **Folic Acid**
- High doses of folic acid (5-10mg) may cause gas, poor appetite, and stomach upset. Those with epilepsy should avoid folic acid in high doses, because it may result in increased occurrence of seizures.
- If taking pancreatic enzymes, which may reduce folic acid absorption, take the two supplements four to six hours apart.

SIDE EFFECTS

There is no side effect in therapeutic doses. When administered for a long period of time manifestation of toxicity may develop.

Contraindications

Hypersensitivity to Cyanocobalamine or any component used, patients with hereditary optic nerve atrophy

Adverse Reactions

- Constipation
- Diarrhoea
- Dark stool
- Nausea
- Epigastric pain, GI irritation
- Long term or excessive administration may cause haemosiderosis

Antidote in the Event of Overdosage

- Symptoms following acute overdoses are usually limited to, nausea, vomiting, and epigastric pain, which are generally reversible with supportive care.

Teratogenicity

- No Known adverse effect on foetus.
- **Presentation and Packaging:**

CODATEMIN (TONIC) is packed in a 200ml amber coloured PVC bottle and screw cap, labeled and packed in a printed laminated chi-board packet.

Shelf Life- 24 months from the date of manufacturer

Storage Condition – Store below 30^0C

(a) Name and Address of Applicant:

STEVEN'S PHARMACEUTICAL LIMITED

6, OKUNOLA STREET, OFF IDIMU ROAD EGBEDA

LAGOS STATE, NIGERIA.

(b) Name and Address of Manufacturer of the Product:

NALIS PHARMACEUTICALS LTD

PLOT R67/68, NEKEDE-NAZE INDUSTRIAL CLUSTER,

NEKEDE OWERRI,

IMO STATE,

NIGERIA.