PROFFESSIONAL INFORMATION

Category D: Complementary Medicine
Health Supplements: D34.12 Multiple Substance Formulation
This unregistered medicine has not been evaluated by SAHPRA for its quality, safety or intended use.
SCHEDULING STATUS: S0

1.NAME OF THE MEDICINE

Bioplus Booster Original Syrup

Caffeine (anhydrous)…….. 90 mg/10 ml
Calcium gluconate……300 mg/10 ml
providing Calcium (elemental)……27,9 mg/10 ml
Calcium citrate……..60 mg/10 ml
providing Calcium (elemental)……12,6 mg/10 ml
Nicotinamide (Vitamin B_3)…….. 8 mg/10 ml
Thiamine hydrochloride (Vitamin B_1)…… 5,33 mg/10 ml
Riboflavin sodium phosphate (Vitamin B_2)…….. 3,67 mg/10 ml
d-Pantothenol (Vitamin B_5)…… 3,66 mg/10 ml
Pyridoxine hydrochloride (Vitamin B_6)…….. 3 mg/10 ml
Cyanocobalamin (Vitamin B_{12}) 0,1 % in mannitol….. 4 µg/10 ml

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 10 ml contains:	
Caffeine (anhydrous)	90 mg
Calcium gluconate providing Calcium (elemental)	300 mg 27,9 mg
Calcium citrate providing Calcium (elemental)	60 mg 12,6 mg
Nicotinamide (Vitamin B_3)	8 mg
Thiamine hydrochloride (Vitamin B_1)	5,33 mg
Riboflavin sodium phosphate (Vitamin B_2)	3,67 mg
d-Pantothenol (Vitamin B_5)	3,66 mg
Pyridoxine hydrochloride (Vitamin B_6)	3 mg
Cyanocobalamin (Vitamin B12) 0,1 % in mannitol	4 µg

Excipients with known effect
Contains sugars: Sucrose 2,40 g/10 ml, Liquid glucose 2,90 g/10 ml
Contains mannitol: 8 mg/ 10 ml
Contains artificial sweeteners: Saccharin sodium 500 1,33 mg/10ml, Sodium cyclamate 13,30 mg/10 ml
Contains alcohol 10,0 % v/v
Preservatives: Methyl parahydroxybenzoate (E218) 0,09 % m/v, Propyl parahydroxybenzoate (E216) 0,01 % m/v
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Syrup.
A clear red, liquid with a cherry brandy odour.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Bioplus Booster Original Syrup is a tonic containing caffeine, the B- vitamins and calcium. Caffeine has been known to increase mental alertness resulting in a rapid and clearer flow of thought. It further reduces the feelings of fatigue and drowsiness resulting in an enhanced state of mind.
The B group vitamins assist in the metabolism of fatty acids, carbohydrates and protein for energy release and production. They are also involved in the maintenance of a healthy nervous system. Calcium assists in muscle contractility as well as myocardial conduction. It also maintains and promotes the growth of strong bones and teeth.

4.2 Posology and method of administration
Posology

Adults over 18 years of age: Take one sachet or 10 ml every eight hours after meals.

Special populations
Paediatric population
Not suitable for use in children and adolescents under 18 years of age.

Method of administration
For occasional use only.
Do not exceed the recommended dosage.
For oral use.
Bioplus Booster Original Syrup should be taken undiluted.
Shake well before use.

4.3 Contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Nicotinamide should not be used in patients with significant hepatic impairment, and other hepato-biliary disorders.
- Cyanocobalamin should not be used for Leber's disease or tobacco amblyopia since these optic neuropathies may degenerate further.
- Calcium should generally be avoided in patients with calcium renal calculi, or a history of renal calculi.
- Calcium citrate should be avoided in patients with renal failure taking aluminium compounds.

4.4 Special warnings and precautions for use

- Large doses of riboflavin result in a bright yellow discoloration of the urine that may interfere with certain laboratory tests.
- Long-term use of large doses of pyridoxine is associated with the development of severe peripheral neuropathies.
- Caution is required when using nicotinamide in patients with active peptic ulcer disease or acute coronary syndrome, patients with or predisposed to gout, or in those who consume large amounts of alcohol.
- Patients with diabetes mellitus should be monitored closely when taking nicotinamide as increases in fasting blood glucose have occurred.
- Calcium should be given with caution to patients with renal impairment, or diseases associated with hypercalcaemia such as sarcoidosis and some malignancies.
- The toxic effects of xanthines (caffeine, theophylline) are additive and use with other xanthine medications should therefore be avoided.
- Caffeine tolerance occurs rapidly to the stimulating effects of caffeine; physical signs of withdrawal including irritability, restlessness, lethargy, and headache may occur if intake is stopped abruptly.
- Avoid caffeine with the use of beta blockers since it can produce bronchospasm.
- Contains sucrose and glucose which may have an effect on the glyceamic control of patients with diabetes mellitus.
- Contains sucrose and glucose: patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take Bioplus Booster Original Syrup.
- Contains glucose which may be harmful to the teeth.
- This health supplement contains 843 mg of alcohol (ethanol) in each dosage unit (10 ml) which is equivalent to 8,43 g/100 ml or 8,43 % w/v. The amount in 10 ml of Bioplus Booster Original Syrup is equivalent to 2 ml of beer or 0.8 ml of wine.
- The amount of alcohol in Bioplus Booster Original Syrup is not likely to have an effect in adults.
- CONTAINS CAFFEINE: Bioplus Booster Original Syrup contains 90 mg of caffeine per dosage unit (10 ml) of syrup. A cup of instant coffee contains approximately 80 mg of caffeine.

- Not suitable for children under the age of 18 years (see section 4.2).
- Total caffeine intake more than 200 mg per day is not recommended during pregnancy and breastfeeding (see section 4.6).
- Consumption with other medicines (e.g., bitter orange extract, synephrine, octopamine, ephedra, ephedrine) which increase blood pressure is not recommended.
- Use of caffeine may result in sleep deprivation.
- Consumption with other caffeine-containing products or foods (e.g., medications, coffee, tea, colas, cocoa, guarana maté) is not recommended.
- Discontinue use two weeks prior to surgery.
- Contains Methyl parahydroxybenzoate (E218) and Propyl parahydroxybenzoate (E216) which may cause allergic reactions (possibly delayed).
- Bioplus Booster Original contains less than 1 mmol sodium (23 mg) per 5 ml, that is to say essentially 'sodium-free'.
- Contains artificial sweeteners: Saccharin sodium 500 1,33 mg/10 ml, Sodium cyclamate 13,30 mg/10ml.

4.5 Interaction with other medicines and other forms of interaction

- Calcium enhances the effects of digitalis on the heart and may precipitate digitalis intoxication.
- Aspirin may reduce the clearance of nicotinamide.
- Use of caffeine with beta-agonists (albuterol, metaproterenol, terbutaline, isoproterenol) can potentiate hypokalaemia.
- Calcium salts reduce the absorption of bisphosphonates (alendronate, ibandronate, risedronate).
- Parenteral chloramphenicol may attenuate the effect of vitamin B12 in anaemia. Use of caffeine with corticosteroids can potentiate hypokalaemia.
- Use of caffeine with diuretics can potentiate hypokalaemia. Calcium salts reduce the absorption of some fluorides.
- Calcium salts reduce the absorption of some fluoroquinolones (ciprofloxacin, gemifloxacin, levofloxacin, moxifloxacin).
- Nicotinamide may increase the requirements for insulin or oral hypoglycaemics.
- Pyridoxine reduces the effects of levodopa, but this does not occur if a dopa decarboxylase inhibitor is also given.
- Serum concentrations of cyanocobalamin may be decreased by the use of oral contraceptives. Pyridoxine decreases serum concentrations of phenytoin.
- Pyridoxine decreases serum concentrations of phenobarbital.
- Although some evidence suggests that combinations of nicotinamide and statins can be given safely, there may be an increased risk of myopathy or rhabdomyolysis.
- Calcium salts reduce the absorption of tetracyclines (doxycycline, minocycline, tetracycline). The two medicines should therefore not be taken within one hour of each other.

Nutrient depletion:

Pyridoxine	Hydralazine, Isoniazid,Penicillamine,Oral contraceptives.
Cyanocobalamin	Neomycin, Aminosalicylic acid, Histamine H2 - antagonists, Omeprazole, Colchicine, Oral contraceptives
Calcium	Corticosteroids
Caffeine	Phenytoin, Phenobarbital, Felbamate, Ethosuximide, Carbamazepine, Valproate, Ritonavir, Rifampicin, and sulfinpyrazone.

Nutrient accumulation:

Calcium	Thiazide diuretics, Vitamin D
Caffeine	Allopurinol, some antiarrhythmics, Cimetidine, Disulfiram, Fluvoxamine, Interferon alfa, Macrolide antibacterials, Quinolones, Oral contraceptives, Tiabendazole, Viloxazine.

Food Interactions

Bran decreases the gastrointestinal absorption of calcium.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety in pregnancy has not been established.

Mothers should closely monitor their intake of caffeine. Caffeine crosses the human placenta but is not considered a teratogen. Foetal blood and tissue levels are similar to maternal concentrations.

Total caffeine intake more than 200 mg per day is not recommended during pregnancy.

Lactation

Safety in lactation has not been established.

Breast milk concentrations of caffeine are thought to be approximately 50 % of maternal serum concentrations and caffeine peaks in milk approximately 1-2 hours after consumption by the

mother.
Total caffeine intake more than 200 mg per day is not recommended during lactation.

Fertility
There are no data on the effects of Bioplus Booster Original Syrup on fertility available.

4.7 Effects on ability to drive and use machines
No studies on the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Adverse effects reported include gastrointestinal disturbances (constipation, bloating and gas), fever, chills, hot flushing, dizziness, malaise, acneform and bullous eruptions, and tremor.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
Excessive amounts of calcium may lead to hypercalcaemia. Symptoms of hypercalcaemia include anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, nephrocalcinosis, renal calculi and, in severe cases, cardiac arrhythmias and coma.

Caffeine overdosage may lead to maniacal behavior, diuresis and repeated vomiting with extreme thirst, tremor, delirium, hyperthermia, tachycardia, tachypnoea, electrolyte disturbances, convulsions and death.

At doses of more than 600 mg per day, caffeine may cause anxiety, tachycardia (rapid heart rate) palpitations, insomnia, restlessness, nervousness, tremor and headache.
Treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Category D: Complementary Medicine
Health Supplements: D34.12 Multiple Substance Formulation

Mechanism of action

- Thiamine is an essential coenzyme for carbohydrate metabolism in the form of the

diphosphate (thiamine pyrophosphate, co-carboxylase).

- Riboflavin is essential for the utilisation of energy from food. The active, phosphorylated forms, flavine mononucleotide (FMN) and flavine adenine dinucleotide (FAD), are involved as coenzymes in oxidative/reductive metabolic reactions.
- Nicotinamide is converted to nicotinamide adenine dinucleotide (nadide) and nicotinamide adenine dinucleotide phosphate (NADP). These co-enzymes are involved in electron transfer reactions in the respiratory chain.
- Pyridoxine is involved mainly in amino acid metabolism but is also involved in carbohydrate and fat metabolism. It is also required for the formation of haemoglobin.
- Cyanocobalamin occurs in the body mainly as methylcobalamin (mecobalamin) and as adenosylcobalamin (cobamamide) and hydroxocobalamin. Mecobalamin and cobamamide act as co-enzymes in nucleic acid synthesis. Mecobalamin is also closely involved with folic acid in several important metabolic pathways.
- Pantothenic acid is a component of co-enzyme A which is essential in the metabolism of carbohydrate, fat, and protein.
- Calcium is essential for nerve transmission, muscle contraction, vascular contraction, vasodilation, glandular secretion, cell membrane and capillary permeability, enzyme reactions, respiration, renal function, and blood coagulation. It also plays a role in neurotransmitter and hormone release and storage, uptake and binding of amino acids, cyanocobalamin (vitamin B_{12}) absorption, and gastrin secretion.
- Caffeine is a methylxanthine that inhibits the enzyme phosphodiesterase and has an antagonistic effect at central adenosine receptors. It is a stimulant of the CNS, particularly the higher centres, and it can produce a condition of wakefulness and increased mental activity. It may also stimulate the respiratory centre, increasing the rate and depth of respiration. Caffeine facilitates the performance of muscular work and increases the total work that can be performed by a muscle.

5.2 Pharmacokinetic properties

- Small amounts of thiamine are well absorbed from the gastrointestinal tract after oral doses, but the absorption of doses larger than about 5 mg is limited. It is widely distributed to most body tissues and within the cell, is mostly present as the diphosphate. 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.
- Riboflavin is readily absorbed from the gastrointestinal tract. It is widely distributed to body tissues; however, little is stored in the body. Riboflavin is converted in the body to the coenzyme flavine mononucleotide (FMN; riboflavin 5'- phosphate) and then to another coenzyme flavine adenine dinucleotide (FAD). About 60% of FMN and FAD are bound to plasma proteins. Riboflavin is excreted in urine, partly as metabolites. As the dose increases, larger amounts are excreted unchanged.
- Nicotinamide is readily absorbed from the gastrointestinal tract after oral doses and widely distributed in the body tissues. The main route of metabolism is conversion to N-methyl nicotinamide and the 2- pyridone and 4-pyridone derivatives; nicotinuric acid is also formed. Small amounts of nicotinamide is excreted unchanged in urine after

therapeutic doses; however, the amount excreted unchanged is increased with larger doses.

- Pyridoxine is readily absorbed from the gastrointestinal tract after oral doses.It is converted to the active forms pyridoxal phosphate and pyridoxamine phosphate. They are stored mainly in the liver where there is oxidation to 4-pyridoxic acid and other inactive metabolites which are excreted in the urine. As the dose increases, proportionally greater amounts are excreted unchanged in the urine.
- Vitamin B_{12} substances bind to intrinsic factor, a glycoprotein 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, with a malabsorption syndrome or with disease or abnormality of the gut, or after gastrectomy. Absorption from the gastrointestinal tract can also occur by passive diffusion; little of the vitamin present in food is absorbed in this manner although the process becomes increasingly important with larger amounts such as those used therapeutically.
- Vitamin B_{12} is extensively bound to specific plasma proteins called transcobalamins; transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. Vitamin B_{12} is stored in the liver, excreted in the bile, and undergoes extensive enterohepatic recycling; part of a dose is excreted in the urine, 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.
- Pantothenic acid is readily absorbed from the gastrointestinal tract after oral doses and is widely distributed in the body tissues. About 70 % of pantothenic acid is excreted unchanged in the urine and about 30 % in the faeces.
- Calcium is absorbed mainly from the small intestine by active transport and passive diffusion. About one-third of ingested calcium is absorbed although this can vary depending upon dietary factors and the state of the small intestine; also, absorption is increased in calcium deficiency and during periods of high physiological requirement such as during childhood or pregnancy and lactation. 1,25-Dihydroxycholecalciferol (calcitriol), a metabolite of vitamin D, enhances the active phase of absorption. Excess calcium is mainly excreted renally. Unabsorbed calcium is eliminated in the faeces, together with that secreted in the bile and pancreatic juice. Minor amounts are lost in the sweat, skin, hair, and nails.
- Caffeine is absorbed readily after oral doses and is widely distributed throughout the body. It passes readily into the CNS and into saliva. In adults, caffeine is metabolised almost completely in the liver via oxidation, demethylation, and acetylation, and is excreted in the urine as 1-methyluric acid, 1- methylxanthine, 7-methylxanthine, 1,7-dimethylxanthine (paraxanthine), 5-acetylamino- 6- formylamino-3-methyluracil (AFMU), and other metabolites with only about 1 % unchanged. Hepatic cytochrome P450 isoenzyme CYP1A2 is involved in caffeine enzymatic metabolism. The elimination half-life is about 3 to 7 hours. The metabolism of caffeine has been shown to be dose dependent with clearance decreasing as the dose is increased suggesting saturable metabolism. Four- to five-fold differences in plasma half-lives of caffeine are common among healthy people. The plasma half-life of caffeine is decreased by smoking and by exercise and is increased by liver disease such as cirrhosis and viral

hepatitis, and in pregnancy. The plasma half-life of caffeine is not affected by old age or obesity. Drug interactions also affect the pharmacokinetics of caffeine, see section 4.5.

5.3 Preclinical safety data
Data on carcinogenicity, genotoxicity and reproductive toxicity testing are not available.

6.PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Sucrose
Liquid Glucose (43 Neutral)
Sodium Chloride BP
Saccharin Sodium 500
Mannitol (E421) [Cyanocobalamin (Vitamin B12) 0,1 % in mannitol]
Sodium Cyclamate
Citric Acid Monohydrate
Hydrochloric Acid 32 % (pH adjustment)
Ethanol 96,5 %
Methyl parahydroxybenzoate (E218)
Propyl parahydroxybenzoate (E216)
Cherry Brandy Liquid Flavour G2292
Colour Raspberry Red H1277
Purified Water

6.2 Incompatibilities
Not applicable

6.3 Shelf life
2 years

6.4 Special precautions for storage
Store in a cool, dry place at or below 25 °C. Protect from light.

6.5 Nature and contents of container
10 ml sachets (laminated plastic/foil) containing 10 ml of a clear red, liquid with a cherry brandy odour.
30 ml bottles (amber glass) containing 30 ml of a clear red liquid with a cherry-brandy flavour.
Pack sizes: 10 ml and 30 ml. Not all pack sizes may be marketed.

6.6 Special precautions for disposal
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Adcock Ingram Limited
1 New Road
Erand Gardens
Midrand
1685
Customer Care: 0860 ADCOCK/232625

8. REGISTRATION NUMBER

To be allocated

9. DATE OF FIRST AUTHORISATION

Not applicable.

10. DATE OF REVISION OF THE TEXT

15 August 2023

adcock ingram

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