	Biomedical Limited, **1, Ohimege Road, Industrial Estate, Ga-Imam, Ilorin, Kwara State**		
	Doc No. BML/BVT/S010	**Date rev 09/2020**	**Next rev date: 08/2025**

Summary of Product Characteristics

For

Bradvite M syrup

(Vitamin A Vitamin B1+Vitamin B2+Vitamin B12+Vitamin C+ Vitamin D)

1. NAME OF MEDICINAL PRODUCT

Bradvite M syrup

2. QUALITATIVE AND QUANTITATIVE DESCRIPTION

Each 5ml of the syrup contains Vitamin A BP 1000I.U

Vitamin B1 BP	1500mcg
Vitamin B2 BP	1500mcg
Vitamin B12 BP	2500mcg
Vitamin C BP	40mg
Vitamin D BP	200I.U
Nicotinamide BP	10mg

3. PHARMACEUTICAL FORM

A brown syrupy viscous liquid with orange and pineapple flavor in 100ml amber PET bottle with pilfer proof cap and graduated dose measurement cap to facilitate easy dosing

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Supply of vitamins corresponding to the daily needs of adults and children over 11 years requiring multi-vitamin supplementation by the parenteral route when oral nutrition is contraindicated, impossible or insufficient (e.g. due to malnutrition, gastrointestinal malabsorption, parenteral nutrition, etc).

4.2 Posology and method of administration

Posology

Bradvite M may be included in the composition of nutritive mixtures combining carbohydrates, lipids, amino acids and electrolytes provided that compatibility and stability have been confirmed for each nutritive mixture, to meet nutrient needs and prevent deficiencies and complications from developing.

The total vitamin amounts from all sources such as nutritional sources, other vitamin supplements, or medications that contain vitamins as inactive ingredients should be considered.

The patient's clinical status and vitamin levels should be monitored to ensure maintenance of adequate levels.

It should be taken into account that some vitamins, especially A, B2, and B6 are sensitive to ultraviolet light (e.g., direct or indirect sun light). In addition, loss of vitamins A, B1, C, and E may increase with higher levels of oxygen in the solution. These factors should be considered if adequate vitamin levels are not achieved.

Method of Administration

Age group	**Dose**
6months-1yr	5-10ml daily
1-5yr	5ml-15ml daily
5-10yrs	10-25ml daily

Or as directed by the physician.

4.3 Contraindications

Bradvite M must not be used in:

- hypersensitivity to the active substances, especially vitamin B1 or to any of the excipients including soy protein/products (lecithin in mixed micelle is soy-derived) or peanut protein/products,

- hypervitaminosis from any vitamin contained in this formulation,

4.4 Special warnings and Precautions for Use

Hypersensitivity Reactions

• Severe systemic hypersensitivity reactions have been reported with Cernevit, other multivitamin preparations, and individual vitamins (including B1, B2, B12 and folic acid). Reactions with fatal outcome have been reported with Cernevit and other parenteral vitamin products (See Section 4.8).

• Cross-allergic reactions between soybean and peanut proteins have been observed.

• In some cases, the manifestations of a hypersensitivity reaction during intravenous administration of multivitamins may be rate related. If infused intravenously, Cernevit should be administered slowly. If injected intravenously, the injection must be administered slowly (over at least 10 minutes).

• The infusion or injection must be stopped immediately if signs or symptoms of a hypersensitivity reaction develop.

Vitamin Toxicity

• The patient's clinical status and blood vitamin concentrations should be monitored to avoid overdose and toxic effects, especially with vitamins A, D and E, and in particular in patients who receive additional vitamins from other sources or use other agents that increase the risk of vitamin toxicity.

• Monitoring is particularly important in patients receiving long-term supplementation.

Hypervitaminosis A

• The risk for hypervitaminosis A and vitamin A toxicity (e.g., skin and bone abnormalities, diplopia, cirrhosis) is increased in, for example:

-patients with protein malnutrition,

-patients with renal impairment (even in the absence of vitamin A supplementation),

-patients with hepatic impairment,

-patients with small body size (e.g., paediatric patients), and

-patients on chronic therapy.

• Acute hepatic disease in patients with saturated hepatic vitamin A stores can lead to the manifestation of vitamin A toxicity.

Refeeding Syndrome in Patients Receiving Parenteral Nutrition

Refeeding severely undernourished patients may result in refeeding syndrome that is characterized by the shift of potassium, phosphorus, and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intakes while avoiding overfeeding can prevent these complications. Should nutrient deficiencies occur, appropriate supplementation may be warranted.

Precipitates in Patients Receiving Parenteral Nutrition

Pulmonary vascular precipitates have been reported in patients receiving parenteral nutrition. In some cases, fatal outcomes have occurred. Excessive addition of calcium and phosphate increases the risk of the formation of calcium phosphate precipitates. Precipitates have been reported even in the absence of phosphate salt in the solution. Precipitation distal to the in-line filter and suspected precipitate formation in the blood stream have also been reported.

In addition to inspection of the solution, the infusion set and catheter should also periodically be checked for precipitates.

If signs of pulmonary distress occur, the infusion should be stopped and medical evaluation initiated.

PRECAUTIONS

Hepatic Effects

• Monitoring of liver function parameters is recommended in patients receiving Bradvite M. Particularly close monitoring is recommended in patients with hepatic jaundice or other evidence of cholestasis.

In patients receiving Bradvite M, instances of liver enzyme increases have been reported, including isolated alanine aminotransferase (ALT) increases in patients with inflammatory bowel disease.

In addition, an increase in bile acid levels (total and individual bile acids including glycocholic acid) have been reported in patients receiving Bradvite M.

• Hepatobiliary disorders including cholestasis, hepatic steatosis, fibrosis and cirrhosis, possibly leading to hepatic failure, as well as cholecystitis and cholelithiasis are known to develop in some patients on parenteral nutrition (including vitamin supplemented parenteral nutrition). The etiology of these disorders is thought to be multifactorial and may differ between patients. Patients developing abnormal laboratory parameters or other signs of hepatobiliary disorders should be assessed early by a clinician knowledgeable in liver diseases in order to identify possible causative and contributory factors, and possible therapeutic and prophylactic interventions.

Use in Patients with Impaired Hepatic Function

Patients with hepatic impairment may need individualized vitamin supplementation. Particular attention should be placed on preventing vitamin A toxicity, because the presence of liver disease is associated with increased susceptibility to vitamin A toxicity, in particular in combination with chronic excessive alcohol consumption (See also Hypervitaminosis A and Hepatic Effects above).

Use in Patients with Impaired Renal Function

Patients with renal impairment may need individualized vitamin supplementation, depending on the degree of renal impairment and the presence of concomitant medical conditions. In patients with severe renal impairment, particular attention should be placed on maintaining adequate vitamin D status and preventing vitamin A toxicity, which may develop in such patients with low-dose vitamin A supplementation or even without supplementation.

Pyridoxine (vitamin B6) hypervitaminosis and toxicity (peripheral neuropathy, involuntary movements) have been reported in patients on chronic haemodialysis receiving intravenous multivitamins containing 4 mg pyridoxine administered three times a week.

General Monitoring

Clinical status and vitamin levels should be monitored in patients receiving parenteral multivitamins as the only source of vitamins for extended periods of time. It is particularly important to monitor for adequate supplementation of, for example:

• Vitamin A in patients with pressure ulcers, wounds, burns, short bowel syndrome or cystic fibrosis

• Vitamin B1 in dialysis patients

• Vitamin B2 in cancer patients

• Vitamin B6 in patients with renal impairment

• Individual vitamins whose requirements may be increased due to interactions with other medicines.

Deficiency of one or more vitamins must be corrected by specific supplementation.

Vitamin K

Bradvite M does not contain Vitamin K. Vitamin K must be administered separately if necessary.

Use in Patients with Vitamin B12 Deficiency

Evaluation of vitamin B12 status is recommended before starting supplementation with Bradvite M in patients at risk for vitamin B12 deficiency and/or when supplementation with Bradvite M over several weeks is planned.

After several days of administration, both the individual amounts of cyanocobalamin (vitamin B12) and folic acid in Bradvite M may be sufficient to result in an increase in red blood cell count, reticulocyte count, and haemoglobin values in some patients with vitamin B12 deficiency-associated megaloblastic anaemia. This may be masking an existing vitamin B12 deficiency. Effective treatment of vitamin B12 deficiency requires higher doses of cyanocobalamin than provided in Bradvite M.

Folic acid supplementation in patients with vitamin B12 deficiency, who do not also receive vitamin B12, does not prevent the development or progression of neurologic manifestations associated with the vitamin B12 deficiency. It has been suggested that neurologic deterioration may even be accelerated.

When interpreting levels of vitamin B12, it should be taken into account that recent intake of vitamin B12 may result in normal levels despite a tissue deficiency.

Laboratory Test Interferences

Ascorbic acid

Depending on the reagents used, the presence of ascorbic acid in blood and urine may cause false high or low glucose readings in some urine and blood glucose testing systems, including test strips and handheld glucose meters. The technical information for any laboratory test should be consulted to determine the potential interference from vitamins.

Geriatric Use

In general, dosage adjustments for an elderly patient should be considered (reducing the dose and/or extending the dosing intervals) reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or drug therapy.

Driving and Operation of Machinery
Bradvite M does not impart ability to drive or operate machine, so it can be safely administered during these activities.

4.5 Drug Interactions

Interactions between specific vitamins in Bradvite M and other agents should be managed accordingly.

Such interactions include:

• Agents that can cause pseudotumor cerebri (including certain tetracyclines): Increased risk for pseudotumor cerebri by concomitant administration of Vitamin A

• Alcohol (chronic excessive consumption): Increases the risk of vitamin A hepatotoxicity

• Anticonvulsants (phenytoin, fosphenytoin, phenobarbital, primidone): Folic acid supplementation can decrease the anticonvulsant serum concentration and increase seizure risk.

• Antiplatelet agents (e.g., aspirin): Vitamin E can add to the inhibition of platelet function

• Aspirin (high dose therapy): Can reduce folic acid levels by increasing urinary excretion

• Certain anticonvulsants (e.g., phenytoin, carbamazepine, phenobarbital, valproate): Can cause folate, pyridoxine and vitamin D deficiencies

• Certain antiretroviral agents: Decreased vitamin D levels have been associated with, e.g., efavirenz and zidovudine. Decreased formation of the active vitamin D metabolite has been associated with protease inhibitors.

• Chloramphenicol: Can inhibit the haematological response to vitamin B12 therapy

• Deferoxamine: Increased risk of iron-induced cardiac failure due to increased iron mobilization by supraphysiologic vitamin C supplementation. For specific precautions, refer to deferoxamine product information.

• Ethionamide: Can cause pyridoxine deficiency

• Fluoropyrimidines (5-fluorouracil, capecitabine, tegafur): Increased cytotoxicity when combined with folic acid

• Folate antagonists, e.g., methotrexate, sulfasalazine, pyrimethamine, triamterene, trimethoprim, and high doses of tea catechins: Block the conversion of folate to its active metabolites and reduce the effectiveness of supplementation

• Folate antimetabolites (methotrexate, raltitrexed): Folic acid supplementation can decrease the antimetabolite effects

• Levodopa: The content of pyridoxine may interfere with the effects of concurrent levodopa therapy.

• Pyridoxine antagonists, including cycloserine, hydralazine, isoniazid, penicillamine, phenelzine: Can cause pyridoxine deficiency

• Retinoids, including bexarotene: Increase the risk of toxicity when used concomitantly with vitamin A (see section 4.4: Hypervitaminosis A)

• Theophylline: Can cause pyridoxine deficiency

• Tipranavir oral solution: Contains 116 IU/mL of vitamin E, which is in excess of the daily recommended intake

• Vitamin K antagonists (e.g., warfarin): Enhanced anticoagulant effect by vitamin E

Drugs that Bind to alpha1-Acid Glycoprotein (AAG):

In an in vitro study using human serum, concentrations of glycocholic acid approximately 4 times higher than the glycocholic acid serum concentration that would result from a bolus injection of Bradvite M in adults, increased the unbound fraction of selected drugs known to bind to alpha1-acid glycoprotein (AAG) by 50-80%.

It is not known whether this effect is clinically relevant if the amount of glycocholic acid contained in a standard Bradvite M dose (as a component of the mixed micelles) is administered by slow intravenous injection, intramuscular injection, or infused over a longer period of time.

Patients receiving Bradvite M as well as drugs that bind to AAG should be closely monitored for increases in response of these drugs. These include propranolol, prazosin, and numerous others.

Interactions with Additional Vitamin Supplementation:

Some medications can interact with certain vitamins at doses markedly higher than those provided with Cernevit. This should be taken into consideration in patients receiving vitamins from multiple sources, and when applicable, patients should be monitored for such interactions and managed accordingly.

Such interactions include:

• Amiodarone: Concomitant use of vitamin B6 can enhance amiodarone-induced photosensitivity

• Agents with anticoagulant effects (e.g., such as abciximab, clopidogrel, heparin, warfarin): Increased bleeding risk due to additional risk of bleeding associated with high vitamin A doses

• Carbamazepine: Inhibition of metabolism associated with large nicotinamide doses

• Chemotherapeutic agents that rely on the production of reactive oxygen species for their activity: Possible inhibition of chemotherapy activity by the antioxidant effects of high doses of vitamin E

• Insulin, antidiabetic agents: Decreased insulin sensitivity associated with large nicotinamide doses

• Iron: High dose-supplementation with vitamin E may reduce the haematological response to iron in anaemic patients

• Oral contraceptives (combination hormone types): High doses of vitamin C have been associated with breakthrough bleeding and contraceptive failure

• Phenobarbital: Increased metabolism/lower serum levels and reduced effect associated with large pyridoxine doses

• Phenytoin, fosphenytoin: Lower serum levels associated with large pyridoxine doses

• Primidone: Decreased metabolism to phenobarbital and increased primidone levels associated with large nicotinamide doses

4.6 Pregnancy and Lactation

Pregnancy

This medicinal product may be prescribed during pregnancy if required, providing the indication and dosages are observed in order to avoid vitamin overdose.

Lactation

Use is not recommended during breastfeeding because of the risk of vitamin A overdose in the neonate.

4.7 Effects on ability to drive and use machine

There is no information on the effects of Bradvite M on the ability to operate an automobile or other heavy machinery.

4.8 Undesirable effects

Adverse drug reactions (ADRs) that have been reported to have occurred after administration of ingredients of Bradvite M syrup are presented with their relative frequencies

Frequencies of ARs are reported, using the following convention: very common (≥ 1/10); common (≥ 1/100 to <1/10); uncommon (≥ 1/1000 to <1/100); rare (≥ 1/10000 to <1/1000); very rare (<1/10000); and unknown (cannot be estimated from the available data).

System Organ Class	Term	Frequency[1]
Immune system disorders	Systemic hypersensitivity reactions with manifestations such as respiratory distress, chest discomfort, throat tightness, urticaria, rash, erythema, epigastric discomfort, as well as cardiac arrest with fatal outcome	Unknown
Metabolism and nutrition disorders	Vitamin A increased[2,3], Retinol binding protein increased[b]	Unknown Unknown
Nervous system disorders	Dysgeusia (metallic taste)	Unknown
Cardiac disorders	Tachycardia	Unknown
Respiratory, thoracic and mediastinal disorders	Tachypnea	Unknown
Gastrointestinal disorders	Nausea	Uncommon

	Vomiting Diarrhoea	Uncommon Unknown
Hepatobiliary disorders	Transaminases increased, Isolated alanine aminotransferase increased[4], Glutamate dehydrogenase increased, Blood alkaline phosphatase increased, Bile acids increased[5] Gamma-glutamyltransferase increased	Unknown Unknown Unknown Unknown Unknown Unknown
Skin and subcutaneous tissue disorders	Pruritus	Unknown
General disorders and administration site conditions	Injection/Infusion Site Pain Pyrexia, Generalized aching, infusion site reactions, i.e., burning sensation, rash	Common Unknown Unknown Unknown

4.9 Overdose

Acute or chronic overdose of vitamins (in particular A, B6, D, and E) can cause symptomatic hypervitaminosis.

The risk of overdose is particularly high if a patient receives vitamins from multiple sources and overall supplementation of a vitamin does not match the patient's individual requirements, and in patients with increased susceptibility to hypervitaminosis (see section 4.4).

Treatment of vitamin overdose usually consists of withdrawal of the vitamin and other measures as clinically indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Vitamins

Balanced association of all water soluble and fat soluble, vitamins essential for the metabolism of the adult and the child aged over 11 years, with the exception of Vitamin K.

5.2 Pharmacokinetics Properties

Not Applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sucrose, Methyl paraben, Xanthan gum, Polysorbate 80, Glycerol, Pineaple flavour, Sweet orange flavour

6.2 Incompatibilities

Biothazine should not be mixed with any other medicinal products, as compatibilities study has not been carried out

6.3 Shelf life

2 years

6.4 Special Precautions for Storage

Bradvite M should be stored in a cool dry place at temperatures not more than 30^{o}C

6.5 Nature and Contents of Container

Plain Amber-coloured Polyethylene terephthalates (PET) bottle with ROPP cap placed inside a paperboard carton

6.6 Special Precautions for disposal

Container and/or any unused product should be disposed in accordance with the local requirement

7. MANUFACTURER

BIOMEDICAL LTD
1, Ohimege Road, Industrial Estate
Ilorin Kwara State, PMB 1449