Summary of Product Characteristics (SPC)

SUMMARY OF PRODUCT CHARACTERISTICS
DR. MEYER'S BECOMBION TABLET

1. NAME OF THE MEDICINAL PRODUCT

Dr. Meyer's Becombion Tablets (Thiamine Hydrochloride (Vit. B1) 5mg, Riboflavin (Vit. B2) 2mg, Pyridoxine Hydrochloride (Vit. B6) 2mg, Nicotinamide (Vit. B3) 20mg)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:

Thiamine Hydrochloride (Vit. B1) 5mg
Riboflavin (Vit. B2) 2mg
Pyridoxine Hydrochloride (Vit. B6) 2mg
Nicotinamide (Vit. B3) 20mg

For a full list of excipients see Section 6.1.

3. PHARMACEUTICAL FORM

Tablet.

Yellow circular shaped tablets with 'B.CO' inscribed on one side and 'FM' on the other side presented in white HDPE plastic securi container with red screw cap containing 100 tablets with insert.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of Vitamin B deficiency

4.2 Posology and method of administration

1 tablet to be taken two or three times daily after food or as prescribed by the physician.

4.3 Contraindications

Hypersensitivity to any of its ingredients.

4.4 Special warnings and precautions for use

Problems in humans have not been documented with intake of normal daily requirements of vitamins during pregnancy nor lactation. However, in the individual case, consult the doctor before taking this medication.

4.5 Interaction with other medicinal products and other forms of interaction

Although the clinical importance is unknown, thiamine reportedly may enhance the effect of neuromuscular blocking agents.

Niacin reportedly potentiates the hypotensive effect of ganglionic blocking drugs.

Patients treated with L-Dopa should not take high doses of pyridoxine (vitamin B6) and thus not **Dr. Meyer's Becombion Tablets**, as pyridoxine reduces the effects of L-Dopa.

4.6 Pregnancy and lactation

Use in pregnancy & lactation: No risks have become known associated with the use of **Dr. Meyer's Becombion Tablets** during pregnancy at the recommended dosage.

Vitamins B1 and B6 are secreted into human breast milk, but risks of overdose for the infant are not known. In individual cases, high doses of vitamin B6 ie, >600 mg daily, may inhibit the production of breast milk.

4.7 Effects on ability to drive and use machines

None reported.

4.8 Undesirable effects

Hypersensitivity reactions predominantly in the form of cutaneous manifestations very rarely occur.

4.9 Overdose

Long-term use of large doses of pyridoxine is associated with the development of severe peripheral neuropathies; the dose at which these occur is controversial.

No cases of deliberate overdosage have been reported with Thiamine. Serious toxicity is

unlikely, even with a massive acute overdose, and specific treatment is unlikely to be required.

No cases of overdose have been described, and it is unlikely that any harm would result.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties ATC Code: A11DB

Thiamine, in the form of thiamine pyrophosphate (also known as cocarboxylase), is the coenzyme for decarboxylation of a-ketoglutaric acid and pyruvic acid.
Thiamine pyrophosphate is also the coenzyme of transketolase. In thiamine deficiency, the hexose monophosphate pathway of glucose oxidation is retarded at the level of the transketolase, so pentose sugars accumulate to three times the normal levels. Thiamine deficiency affects the peripheral nervous system, the gastrointestinal tract, and the cardiovascular system. This vitamin is necessary for the optimal growth of infants and children.

Riboflavin (B_2) plays a vital role in cellular respiratory reactions in conjunction with niacinamide.

Vitamin B6 has two main active derivatives, i.e. pyridoxal and pyridoxamine, whereas inactive forms include norvitamin B6, 4-pyridoxic acid, and 5-pyridoxic acid. Vitamin B6 is antagonized by various drugs such as 4-deoxypyridoxine, 4-methoxypyridoxine, toxopyrimidine, penicillamine, semicarbazide, and isoniazid. 4 Pyridoxal and pyridoxamine phosphate are mainly involved as co-enzymes, especially in the metabolic transformation of amino acids including decarboxylation, transamination and racemization.
In the metabolism of tryptophan, vitamin B6 is involved in a number of enzymatic reactions.
In vitamin B6-deficient humans and animals, a number of metabolites of tryptophan, especially xanthurenic acid, are excreted in urine in abnormally large quantities. 5 Pyridoxine deficiency in rats is accompanied by a lowered threshold for electroshock-induced tonic'clonic seizures. This is reversed by pyridoxine. The tryptophan loading test has been used to assess vitamin B6 status. This test is based on the reduction in kynureninase activity owing to a deficiency of its cofactor, pyridoxal phosphate. The excretion, specifically of xanthurenic acid and possibly also of kynurenine and hydroxy-kynurenine, is measured before and after administration of a dose of tryptophan (l-

tryptophan 10 g or 100 mg.kg^{-1} body weight) using a 24-h collection of urine. A lower suggested dose of tryptophan (2 g) does not produce sufficient challenge to the pathway tested. The tryptophan load test is not a reliable indicator of vitamin B6 status in persons receiving estrogens or with increased secretion of glucocorticoids.

Vitamin B6 is a cofactor in the conversion of tryptophan to 5-hydroxytryptamine (5-HT) and of methionine to cysteine. 8 Pyridoxine is capable of modifying the action of steroid hormones in vivo by interacting with the steroid'receptor complexes. Biochemical interaction occurs between pyridoxal phosphate and certain drugs and toxins.

Isoniazid increases urinary excretion of vitamin B6, and prolonged use of penicillamine has caused deficiency of vitamin B6. The drugs cycloserine and hydralazine are also antagonists of vitamin B6. Administration of the vitamin reduces the neurological side effects associated with the use of these agents.

Niacinamide (nicotinamide) plays a vital role in cellular respiration in conjunction with riboflavin 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 appears in breast milk. Within the cell, thiamine 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.
Pyridoxine, 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. 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. Pyridoxal crosses the placenta and is distributed into breast milk.

5.2 Preclinical safety data

Beagles receiving a daily dose of 300 mg.kg-1 pyridoxine hydrochloride developed a swaying gait within 9 days. They eventually became unable to walk but were not weak. 14 Hoover and others 15 reported a similar observation in beagles. Pyridoxine in doses of 150 mg.kg-1 body weight given daily for 100 days caused degeneration of the central tracts arising from the spinal and trigeminal ganglia.

Rats receiving large doses of pyridoxine developed gait ataxia that subsided after vitamin B6 was withdrawn. Axonal degeneration of the sensory fibre system was observed. The fibers derived from the ventral root were spared although the degeneration approached the dorsal root ganglia. Neurons in the ganglia did not degenerate. There are no reported studies of reproductive toxicity, teratogenic effects, carcinogenicity, or mutagenicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Nipagin (Methyl Paraben), Nipasol (Propyl Paraben), Citric Acid Anhydrous, Lactose, Gelatin, Corn Starch (Bulk), Corn Starch (Paste), Talcum, Magnesium Stearate, Purified Water

6.2 Incompatibilities

None reported.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at temperature not exceeding 30°C, in dry place.

6.5 Nature and contents of container

White HDPE plastic securi container with red screw cap containing 100 tablets with insert

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Farmex Meyer Ltd.,

Km 38, Lagos–Abeokuta Express Road,

Sango-Ota, Ogun State,

Nigeria.