1.3.1 PRESCRIBING INFORMATION

SUMMARY OF PRODUCT CHARACTERISTICS.

1. NAME OF THE PRODUCT:

FOLIC ACID PLUS

VITAMIN B12 TABLETS

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Folic Acid ……5mg
Vitamin B12……..5mcg

3. PHARMACEUTICALFORM:

Suspension

4. CLINICALPARTICULARS

4.1. TherapeuticIndications

For the treatment of folate-deficient megaloblasticanaemia due to malnutrition, malabsorption syndromes (such as coeliac disease or sprue) and increased utilisation as in pregnancy.

Posology and method ofadministration

Folic Acid

ADULTS

For nutritional megaloblastic anaemia: a dose of 1 tablet daily for up to 4 months is normally sufficient but up to 15 mg daily may be required where malabsorption exists.

A maintenance dose of 5 mg every 1 to 7 days may also be required.

CHILDREN

In children over 1 year the dose is as for adults. (See BNF 25).

Vit B12

Pernicious Anemia:Vitamin B_{12} is the recommended treatment and will be required for the remainder of the patient's life. The oral form is not dependable. A dose of 100 mcg daily for 6 or 7 days should be administered by intramuscular or deep subcutaneous injection. If there is clinical improvement and if a reticulocyte response is observed, the same amount

may be given on alternate days for seven doses, then every 3 to 4 days for another 2 to 3 weeks. By this time hematologic values should have become normal. This regimen should be followed by 100 mcg monthly for life. Folic acid should be administered concomitantly if needed.

4.2 Contraindications

FOLIC ACID

Hypersensitivity to the active substance or to any of the excipients listed.

• Long-term folate therapy is contraindicated in any patient with untreated cobalamindeficiency. This can be untreated pernicious anaemia or other cause of cobalamin deficiency, including lifelong vegetarians. In elderly people, a cobalamin absorption test should be done before long-term folate therapy. Folate given to such patients for 3 months or longer has precipitated cobalamin neuropathy. No harm results from short courses of folate

• Folic acid should never be given alone in the treatment of Addisonian pernicious anaemia and other vitamin B_{12} deficiency states because it may precipitate the onset of subacute combined degeneration of the spinal cord

• Folic acid should not be used in malignant disease unless megaloblasticanaemia owing to folate deficiency is an important complication.

VITAMIN B12

Sensitivity to cobalt and/or vitamin B_{12}

4.3 Special warnings and precautions for use

FOLIC ACID

. Patients with vitamin B_{12} deficiency should not be treated with folic acid unless administered with adequate amounts of hydroxocobalamin, as it can mask the condition but the subacute irreversible damage to the nervous system will continue. The deficiency can be due to undiagnosed megaloblastic anaemia including in infancy, pernicious anaemia or macrocytic anaemia of unknown aethiology or other cause of cobalamin deficiency, including lifelong vegetarians.

Caution should be exercised when administering folic acid to patients who may have folate dependent tumours.

This product is not intended for healthy pregnant women where lower doses are recommended, but for pregnant women with folic acid deficiency or women at risk for the reoccurrence of neural tube defect.

Folic Acid Tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Folic Acid Tablets contain sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

VITAMIN B12

Vitamin B_{12} deficiency that is allowed to progress for longer than 3 months may produce permanent degenerative lesions of the spinal cord. Doses of folic acid greater than 0.1 mg per day may result in hematologic remission in patients with vitamin B_{12} deficiency. Neurologic manifestations will not be prevented with folic acid, and if not treated with vitamin B_{12}, irreversible damage will result.
Doses of cyanocobalamin exceeding 10 mcg daily may produce hematologic response in patients with folate deficiency. Indiscriminate administration may mask the true diagnosis.

4.4 Interaction with other medicinal products and other forms of interaction

There is a specific interaction between phenytoin and folate such that chronic phenytoin use produces folate deficiency. Correction of the folate deficiency reduces plasma phenytoin with potential loss of seizure control. Similar but less marked relationship exist with all anti-convulsant treatments including sodium valproate, carbamazepine and the barbiturates. Sulphasalazine and triamterene also inhibit absorption.

Antibacterials, chloramphenicol and co-trimoxazole, may interfere with folate metabolism.

Folate supplements enhance the efficacy of lithium therapy. Methotrexate and trimethoprim are specific anti-folates and the folate deficiency caused by their prolonged use cannot be treated by Folic Acid Tablets BP. Folinic acid should be used. Nitrous oxide anaesthesia may cause an acute folic acid deficiency. Both ethanol and aspirin increase folic elimination.

4.5 Pregnancy and lactation

FOLIC ACID
Pregnancy

There are no known hazards to the use of folic acid in pregnancy, supplements of folic acid are often beneficial.

Non-drug - induced folic acid deficiency, or abnormal folate metabolism, is related to the occurrence of birth defects and some neural tube defects. Interference with folic acid metabolism or folate deficiency induced by drugs such as anticonvulsants and some antineoplastics early in pregnancy results in congenital anomalies. Lack of the vitamin or its metabolites may also be responsible for some cases of spontaneous abortion and intrauterine growth retardation.

Lactation

Folic acid is actively excreted in human breast milk. Accumulation of folate in milk takes precedence over maternal folate needs. Levels of folic acid are relatively low in colostrum but as lactation proceeds, concentrations of the vitamin rise. No adverse effects have been observed in breast fed infants whose mothers were receiving folic acid.

VITAMIN B12

Pregnancy

Pregnancy Category C: Adequate and well-controlled studies have not been done in pregnant women. However, vitamin B_{12} is an essential vitamin and requirements are increased during pregnancy. Amounts of vitamin B_{12} that are recommended for pregnant women (4 mcg daily) should be consumed during pregnancy.

4.6 Undesirableeffect.

Gastrointestinal disorders Rare (≥1/10,000 til <1/1,000)	Anorexia, nausea, abdominal distension and flatulence
Immune system disorders Rare (≥1/10,000 til <1/1,000) Not known (frequency cannot be estimated from the available data)	Allergic reactions, comprising erythema, rash, pruritus, urticaria, dyspnoea, and shock. Anaphylactic reaction

5. Pharmacological properties

5.1 Pharmacodynamic properties

FOLIC ACID

Folic acid is a member of the vitamin B group which is reduced in the body to tetrahydrofolate, a co-enzyme active in several metabolic processes and produces a haemopoietic response in nutritional megaloblastic anaemias (but see warning in Section 4.4 regarding need for concomitant use of hydroxycobalamin).

Folic acid is rapidly absorbed and widely distributed in body tissues.

VITAMIN B12

This medicine contain cyanocobalamin vitamin B 12, which is used for the treatment of pernicious anaemia, and nutritional deficiencies of vitamin B 12 which results in macrocytic anaemia.

5.2 Pharmacokineticproperties

FOLIC ACID

Absorption – folic acid is rapidly absorbed from the gastrointestinal tract, mainly from the proximal part of the small intestine. Dietary folates are stated to have about half the bioavailability of crystalline folic acid. The naturally occurring folate polyglutamates are largely deconjugated and reduced by dihydrofolate reductase in the intestine to form 5-methyltetrahydrofolate (5MTHF). Folic acid given therapeutically enters the portal circulation largely unchanged, since it is a poor substrate for reduction by dihydrofolate reductases.

Distribution – via portal circulation. 5MTHF from naturally occurring folate is extensively plasma bound. The principal storage site of folate is in the liver; it is also actively concentrated in the CSF. Folate is distributed into breast milk.

Metabolism – therapeutically given folic acid is converted into the metabolically active form 5MTHF in the plasma and liver. There is an enterohepatic circulation for folate.

Elimination – Folate metabolites are eliminated in the urine and folate in excess of body requirements is excreted unchanged in the urine. Folic acid is removed by haemodialysis.

VITAMIN B12

Absorption

The absorption of cobalamins from the gut is dependent upon the glycoprotein intrinsic factor.

Distribution

Cobalamins are transported rapidly into the blood bound to protein, known as transcobalamins.

Elimination

Cobalamins are stored in the liver and excreted in the bile. They are known to cross the placenta.

5.3 Preclinical safetydata

There is no pre-clinical data of relevance to a prescriber which is additional to that already included in other sections.

6. Pharmaceuticalparticulars

6.1 List ofExcipients:

Folic Acid

Vitamin B12

Starch

Dicalcium Phosphate

Lactose

Starch(paste)

Gelatin

Methyl Paraben Sodium

Propyl Paraben Sodium.

6.2 ShellfLife:

3 years

6.3 Special Precaution forStorage:

Store in a cool dry place not above 30°C.Protect from light.

6.4 Nature and contents ofcontainer:

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6.5 Special precautions for disposal and otherhandling:

Keep container in the outer carton to protect from light.

7. MARKETING AUTHORISATIONHOLDER

RICHYGOLD INTERNATIONAL LIMITED
103C AMUWO-ODOFIN INDUSTRIAL SCHEME OSHODI APAPA EXPRESS WAY, LAGOS NIGERIA

8. MARKETING AUTHORISATIONNUMBER(S)

None

9. DATEOFFIRSTAUTHORISATION/RENEWALOFTHEAUTHORISATION

Not applicable

RICHYGOLD INTERNATIONAL LIMITED

COMMON TECHICAL DOCUMENTS

Product Name= FOLIC ACID PLUS VITAMIN B12 TABLETS
Generic Name= Folic Acid 5mg, Vitamin B12 5mcg.