National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC) TEMPLATE

1. NAME OF THE MEDICINAL PRODUCT

Galways Folic plus Vitamin B12 Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Folic Acid 5mg
Vitamin B12 (as Cyanocobalamin) 5mcg.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Yellow uncoated tablets.

4. Clinical particulars

4.1 Therapeutic indications

1. Folic acid and Vitamin B_{12} are important erythropoietic factors, which aid in the buildup of haemoglobin and blood enrichment
2. Treatment of nutritional folic acid and Vitamin B_{12} deficiency and as a supplement in pregnancy and disease.
3. Treatment of and prevention of megaloblastic and pernicious anaemias when parenteral administration is not possible or not advised.
4. For the prevention of neural tube defects in offsprings of pregnant women
5. Treatment of tropical sprue.

4.2 Posology and method of administration

Posology

Adults (including the elderly)

Usual Dose: one tablet daily to be taken after food or as directed by physician.

Paediatric population

One tablet daily to be taken after food or as directed by physician.

Method of administration

For oral administration.

4.3 Contraindications

This medicinal product is contraindicated in:

- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Folic acid should not be used in malignant disease unless megaloblastic anaemia owing to folate deficiency is an important complication.
- Cyanocobalamin should not be used for Leber's disease or tobacco amblyopia since these optic neuropathies may degenerate further.

4.4 Special warnings and precautions for use

- For pernicious anaemia, an adequate dose must be used and the blood picture must be examined regularly at least every three months for 18 months until stabilised, and then annually.
- Indiscriminate administration of this medicine may mask precise diagnosis.

- Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.
- 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 defects.

4.5 Interaction with other medicinal products and other forms of interaction

FOLIC ACID

- 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 (including phenobarbital and primidone). Sulphasalazine and triamterene also inhibit absorption.
- Antibacterials – chloramphenicol and co-trimoxazole may interfere with folate metabolism.
- Folic acid may interfere with the toxic and therapeutic effects of methotrexate. Methotrexate and trimethoprim are specific anti-folates and the folate deficiency caused by their prolonged use cannot be treated by Folic Acid Tablets BP.
- Folate supplements enhance the efficacy of lithium therapy.
- Folinic acid should be used.
- Nitrous oxide anaesthesia may cause an acute folic acid deficiency.
- Both ethanol and aspirin increase folic elimination.

VITAMIN B12

- Absorption may be reduced by Para-aminosalicylic acid, colchinine, biguanides, neomycin, cholestyramine, potassium chloride, methyldopa, and cimetidine.
- Patients treated with chloramphenicol may respond poorly to this medicine.
- Serum levels of this medicine may be lowered by oral contraceptives. These interactions are unlikely to have clinical significance.
- Anti-metabolities and most antibiotics invalidate vitamins B12 assays by microbiological techniques.

4.6 Pregnancy and Lactation

Pregnancy
No teratogenic effect has been reported with the use of Folic acid or Cyanocobalamin in pregnant women rather it is beneficial in the prevention of neural tube defects in the foetus.

Breast-feeding
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.

4.7 Effects on ability to drive and use machines
None.

4.8 Undesirable effects

Gastrointestinal disorders Rare (≥1/10,000 to <1/1,000)	Anorexia, nausea, abdominal distension and flatulence
Immune system disorders Rare (≥1/10,000 to <1/1,000)	Allergic reactions, comprising erythema, rash, pruritus, urticaria, dyspnoea, and anaphylactic reactions (including shock).

4.9 Overdose

Overdosage is unlikely to require treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code BO3B B01/ B03BA01

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.
It is used in the treatment and prevention of folate deficiency states.

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

5.2 Pharmacokinetic properties

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.

Biotransformation
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 safety data
No further relevant data.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Microcrystalline Cellulose
Maize Starch
Lactose
Stearic Acid

6.2 Incompatibilities
None stated.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Store above 30°C in a dry place.
Protect from light.

6.5 Nature and contents of container
The tablets are packed in opaque plastic containers (securitainers) composed of either high density polypropylene or high density polyethylene with a tamper-evident closure composed of high density polyethylene with a packing inclusion of a silica desiccant pack.
Pack size: 10 x 10, 100 and 1000 tablets.

6.6 Special precautions for disposal
Not applicable.

7 APPLICANT/MANUFACTURER

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