PROFESSIONAL INFORMATION

Scheduling Status: S0

1. Proprietary Name

Folate with Quatrefolic®

2. Qualitative and Quantitative Composition

Each capsule contains the composition as per table 2.1 below.

2.1 Composition

Each capsule contains:

Quatrefolic® (as Glucosamine Salt of 6-S-5-Methyltetrahydrofolate (MTHF))	740 ug
Providing 400 ug elemental folate	

Other ingredients: milled rice.

2.2 Sugar free. Free from gelatine, dairy, soy, synthetic fillers, gluten, preservatives, and artificial colourants. GMO-free and suitable for vegans.

2.3 For full list of excipients see section 7.1.

3. Pharmaceutical Form

Thirty white size 0 capsules containing light brown coloured powder.

4. Clinical Information

4.1 Indications for Use

Contributes to normal development of maternal tissue and helps prevent neural tube defects during pregnancy, a factor in the production of red blood cells.

4.2 Method of Administration and Posology

4.3

4.3.1 Administration

Orally.

4.3.2 Posology

Adults and children over 18 only.
Take 1 capsule daily with meals.
Take capsule with a sufficient quantity of water.
Do not chew the capsules, swallow whole.
Take capsules at approximately the same time every day.

4.4 Contraindications

Not recommended for individuals who are hypersensitive (allergic) to any of the ingredients used in FoodGrown™© Folate with Quatrefolic®.

4.5 Special Warnings and Precautions

Do not exceed the recommended daily dose.

4.6 Interactions

Fluorouracil: theoretically, high doses of folic acid might increase the toxicity of 5-fluorouracil. Increases in gastrointestinal side effects of 5-fluorouracil, such as stomatitis and diarrhoea, have been described in two clinical studies when leucovorin, a form of folic acid, was administered with 5-fluorouracil.

Capecitabine: use of high-dose folic acid might contribute to capecitabine toxicity. Clinical research suggests that higher serum folate levels are associated with an increased risk for moderate or severe toxicity during capecitabine-based treatment for colorectal cancer. Additionally, in one case report, taking folic acid 15 mg daily might have contributed to increased toxicity, including severe diarrhoea, vomiting, oedema, hand-foot syndrome, and eventually death, in a patient prescribed capecitabine.

Methotrexate: folic acid might reduce the efficacy of methotrexate as a cancer treatment when given concurrently. Methotrexate exerts its cytotoxic effects by preventing conversion of folic acid to the active form needed by cells. There is some evidence that folic acid supplements reduce the efficacy of methotrexate in the treatment of acute lymphoblastic leukemia, and theoretically they could reduce its efficacy in the treatment of other cancers. Advise cancer patients to consult their oncologist before using folic acid supplements. In patients treated with long-term, low-dose methotrexate for rheumatoid arthritis (RA) or psoriasis, folic acid supplements can reduce the incidence of side effects, without reducing efficacy.

Phenobarbital: folic acid might have antagonistic effects on phenobarbital and increase the risk for seizures. Folic acid can have direct convulsant activity in some people, reversing the effects of phenobarbital and worsening seizure control. Monitor closely for increased seizure activity.

Phenytoin: folic acid might reduce serum levels of phenytoin in some patients. Folic acid may be a cofactor in phenytoin metabolism. Folic acid, in doses of 1 mg daily or more, can reduce serum levels of phenytoin in some patients. Increases in seizure frequency have been reported. If folic acid supplements are added to established phenytoin therapy, monitor serum phenytoin levels closely. If phenytoin and folic acid are started at the same time and continued together, adverse changes in phenytoin pharmacokinetics are avoided. Note that phenytoin also reduces serum folate levels.

Primidone: folic acid might have antagonistic effects on primidone and increase the risk for seizures. Folic acid can have direct convulsant activity in some people, reversing the effects of primidone and worsening seizure control. Monitor closely for increased seizure activity. Note that primidone also reduces serum folate levels.

Pyrimethamine: folic acid might antagonize the effects of pyrimethamine. Folic acid can antagonize the antiparasitic effects of pyrimethamine against toxoplasmosis and Pneumocystis carinii pneumonia. Folic acid doesn't antagonize the effects of pyrimethamine in the treatment of malaria because malarial parasites cannot use exogenous folic acid. Use folinic acid as an alternative to folic acid when indicated.

The following drugs may interfere with folic acid interfere with folic acid absorption and reduce serum folate levels.

Alcohol, aminosalicylic acid, carbamazepine, estrogen, h2 Blockers, metformin, methotrexate, methylprednisolone, antibiotic, colestipol, cycloserine, pancreatic enzymes, pentamidine, phenobarbital, phenytoin, PPI, pyrimethamine, retinoids, sulfasalazine, triamterene, trimethoprim, and valproate.

Aspirin: might affect folate protein binding and affect folate excretion.

Cycloserine: might reduce serum folate levels and increase the risk of folate deficiency.

Diuretics: might increase folate excretion; however, the clinical significance of this is unclear.

Interactions with supplements:

Green Tea: might increase the activity of folate.

Interaction with conditions:

Angioplasty: there is some concern that B vitamins might increase the rate of restenosis after bare metal stent placement. An intravenous loading dose of folic acid, vitamin B6 and vitamin B12, followed by oral administration of folic acid 1.2 mg, vitamin B6 48 mg, and vitamin B12 60 ug daily after coronary stenting might actually increase restenosis rates. Due to the potential for harm, this combination of vitamins should not be recommended for patients receiving coronary stents.

Cancer: there is some concern that folic acid might increase the risk of certain cancers. Preliminary clinical research suggests folic acid in doses of 0.8 – 1 mg daily might increase the risk of cancer, possibly by increasing cell growth. However, other research has shown no effect. Until more is known, avoid folic acid in doses higher than the RDA in people with a history of cancer.

Seizure disorder: high supplemental doses of folic acid might exacerbate seizures in people with seizure disorders. Doses less than 1 mg have rarely been associated with increased seizure activity.

Vit B 12 deficiency: there is some concern that folic acid can improve hematologic signs of megaloblastic anemia, without resolving the underlying cause, thereby masking vitamin B12 deficiency. This may allow potentially irreversible neurological damage to progress in patients with vitamin B12 deficiency.

4.6 Pregnancy and Lactation

Safe for individuals who are pregnant or breastfeeding.

4.7 Effects on ability to drive and use machinery.

No known effect.

4.8 Side Effects

No known side effects. Orally, all ingredients are well tolerated.

Serious Adverse Effects (Rare):

Orally*:* may increase risk of cancer (long-term use), cardiovascular complications, liver injury, and seizures.

5 Pharmacological Classification

Category D: 34.11 Vitamins. Complementary Medicine: Health Supplement.

6 Pharmacokinetic Properties

Absorption: folate in food is about 20% to 50% less bioavailable than synthetic folic acid, which is almost 100% bioavailable. Before folate from food can be absorbed, the polyglutamate side chain must undergo enzymatic deconjugation in the small intestine to form the absorbable monoglutamate form. Folate deconjugation occurs maximally at a pH of 6-7. Folate levels in the blood increase approximately 30 minutes following consumption in foods and levels remain elevated for up to 5 hours with no difference in the area under the curve (AUC) for monoglutamyl vs. polyglutamyl folates. The bioavailability of polyglutamyl forms of folic acid appears to be approximately 50% to 78% of monoglutamyl folic acid.

Some vitamin manufacturers claim that supplements containing L-methylfolate are better than folic acid-containing supplements. There is some evidence that L-methylfolate is slightly more bioavailable than folic acid. However, with continuing use of the supplements there is no difference in blood levels. Some manufacturers claim that L-methylfolate is a better alternative to folic acid because some people lack the enzymes to convert folic acid to L-methylfolate. But so far, there is no reliable evidence that this makes a meaningful difference. For example, equivalent doses of folic acid and L-methylfolate raise folate levels in pregnant women equally well.

There is also interest in the reduced form of synthetic folate, L-5-methyltetra-hydrofolate (L-5-MTHF), which is dependent on vitamin B12 for metabolism. A single dose of L-5-MTHF seems to result in faster and greater absorption when compared with folic acid, both in those with the homozygous (TT) MTHFR and the wild-type (CC) MTHFR genotypes. During longer supplementation periods of up to 16 weeks, this increased bioavailability seems to be less pronounced but maintained. Two small clinical studies in females show that taking L-5-MTHF (Metafolin, Eprova) 1.3 mg or L-5-MTHF 416 mcg daily for 12-16 weeks resulted in slightly higher folate concentration in red blood cells when compared with taking the molar equivalent of folate 1 mg or 400 mcg daily for 12-16 weeks .

Distribution: In patients with coronary artery disease, plasma 5-methyltetrahydrofolate increases proportionately with treatment dose of folic acid, whereas vascular tissue 5-methyltetrahydrofolate does not.

Metabolism: After folic acid is absorbed, it is reduced to tetrahydrofolate and then enters a methylation cycle. Tetrahydrofolate is then converted to L-methylfolate. In patients with coronary artery disease, plasma 5-methyltetrahydrofolate increases proportionately with treatment dose of folic acid. However, unmetabolized folic acid is also found in both plasma and breast milk when folic acid is consumed.

Excretion: Folic acid is excreted mainly in the urine; however, it is also found in the faeces. Folate is also lost during haemodialysis.

7 Pharmaceutical Information

7.1 List of Excipients

Vegetarian capsules, milled rice flour.

7.2 Incompatibilities

None.

7.3 Shelf Life

Twenty-four months from date of manufacture.

7.4 Storage

Store in a cool dry place, between 15°C -25°C. Store in original container.

7.5 Presentation

Thirty white capsules packed in a 300 ml cylindrical white container with a lid and packaged in a single carton.

7.6 Disposal and handling of product

All unused medication should be disposed of in accordance with local regulatory authority.

8. Holder of certificate of registration

FoodGrown™©
371 Angus Crescent
Northlands Business Park
Northriding
Gauteng
South Africa

9. Registration Number

Still to be allocated

10. Date of first authorisation

Still to be allocated

11. Date of review

New

12. Reference: https://naturalmedicines.therapeuticresearch.com/

APPLICANT DETAILS:

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