NEW ZEALAND DATA SHEET

FOLIC ACID VIATRIS

1. Product Name

FOLIC ACID VIATRIS, 5 mg, tablet.

2. Qualitative and Quantitative Composition

Each tablet contains 5 mg of folic acid.

Excipient(s) with known effect:

Lactose, maize starch, crospovidone and povidone.

Allergen Declaration: Contains sulfites and sugars as lactose.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

7 mm, flat bevelled edged, yellow tablet with score line on one side and blank on the other.

The score line is not intended for breaking the tablet.

4. Clinical Particulars

4.1 Therapeutic indications

FOLIC ACID VIATRIS 5 mg tablets are indicated for the treatment of megaloblastic anaemia when folate deficiency is identified as the exclusive cause. Folate deficiency is a consequence of inadequate dietary intake, malabsorption, or increased utilisation in conditions such as pregnancy, lactation, haemolytic anaemia, hyperthyroidism, exfoliative dermatitis, and chronic infection.

FOLIC ACID VIATRIS 5 mg tablets are also indicated for prophylaxis of folate deficiency resulting from renal dialysis, pregnancy and lactation when the mother is malnourished, and chronic haemolytic states such as thalassaemia major or sickle-cell anaemia.

4.2 Dose and method of administration

Dose

Approximately 400 micrograms/day of folic acid is considered a suitable average intake. Body stores of folate in healthy people have been reported between 5 to10 mg but could be much higher.

Patients should remain under strict monitoring and the maintenance dose must be adjusted immediately in case of a risk of relapse.

Folate is present, mostly combined with several L(+)-glutamic acid moieties, in many foods, but in particular, liver, kidney, yeast, nuts and leafy green vegetables. Folic acid is readily oxidised to unavailable forms and is easily destroyed during cooking.

As folic acid is easily absorbed, it can be administered orally with good results apart from in exceptionally severe disease or in severe cases of intestinal malabsorption.

In concomitant therapy with antiepileptic drugs, the daily dose of folic acid should be reduced to the lowest effective amount and divided into multiple single doses.

Special populations

Paediatric

FOLIC ACID VIATRIS 5 mg tablets are not suitable for administration to infants aged under 12 months.

Method of administration

Folic acid should not be added to multivitamin preparations as it may lower concentration of vitamin B_{12} in the blood.

FOLIC ACID VIATRIS **5 mg tablets**

- **Folate-deficient megaloblastic anaemia:**

  Adults: An initial dosage of 10-20mg folic acid daily for 14 days is recommended or until a haematopoietic response has been obtained. The daily maintenance dose is 2.5 to 10mg.
  FOLIC ACID VIATRIS cannot meet all dosing regimens.

  Children: 5 to 15mg daily according to the severity of the deficiency.

- **Prophylaxis of folate deficiency:**
  1 tablet (5 mg) taken daily or weekly may be necessary in chronic haemolytic cases such as thalassaemia major or sickle-cell anaemia, depending on the diet and rate of haemolysis.

- **Expected pregnancy:**
  5 mg taken daily for 4 weeks before conception and during the first trimester of pregnancy for women who are at risk of having a pregnancy affected by neural tube defects.

4.3 Contraindications

Hypersensitivity to folic acid or to any of the excipients listed in section 6.1.

Long-term folate therapy is contraindicated in any patient with untreated cobalamin deficiency. 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 B12 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 megaloblastic anaemia owing to folate deficiency is an important complication. The haematological features of vitamin B12 deficiency may be corrected with folic acid but the neurological effects will not be alleviated and may become irreversible.

4.4 Special warnings and precautions for use

The absorption of folic acid and the success of treatment can be impaired in the case of severe deficiency or in severe cases of intestinal malabsorption. Vitamin B12 deficiency needs to be excluded before folic acid is prescribed.

Patients with vitamin B12 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 aetiology or other cause of cobalamin deficiency, including lifelong vegetarian,

Cobalamin deficiency can go undetected for several years, during which time the neuropsychiatric manifestations may become irreversible (and worsen with folate supplementation). Hence, for elderly patients, a cobalamin absorption test should be performed prior to starting long-term folate treatment.

Large doses of folic acid may counteract the anti-epileptic effect of diphenylhydantoin. Patients receiving concurrent administration of diphenylhydantoin and folic acid should be monitored for possible loss of seizure control.

Folic acid does not correct folate deficiency due to dihydrofolate reductase inhibitors, such as methotrexate. Folinic acid should be used for this purpose.

Folic acid should not be added to multivitamin preparations as it may lower the concentration of vitamin B12 in the blood.

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.

This product contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose – galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Folic acid may interact with antacids which contain aluminium or magnesium, antibiotics and cholestyramine, sulphonamides including sulphasalazine and zinc supplements.

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. In such cases, monitor antiepileptic drug concentrations and adjust (increase) their dose accordingly. 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. With decreased serum levels of folate due to antiepileptics, adjustment (increase) of maintenance dose of folic acid may be required depending on the severity of folic acid deficiency.

In patients experiencing haemolytic anaemia or anticonvulsant therapy, it may be necessary to increase the maintenance dose.

Antibacterials – chloramphenicol and co-trimoxazole may interfere with folate metabolism

Folate depletion is a side effect of folate antagonists such as 5-fluorouracil, methotrexate, trimethoprim, pyrimethamine and sulphonamides. Potentially severe deficiencies may be treated with calcium folinate therapy. Methotrexate has a high affinity for mammalian dihydrofolate reductase and therefore inhibits the reduction of folic acid to tetrahydrofolate.

Trimethoprim and pyrimethamine are more selective inhibitors of microbial dihydrofolate reductase, the concentrations required to inhibit the mammalian enzyme are 10,000 to 50,000 times greater than the concentrations required to inhibit the microbial enzyme for trimethoprim and 1,400 times greater for pyrimethamine.

The requirements for folic acid may be increased in patients receiving analgesics, anticonvulsant particularly hydantoin and carbamazepine, oestrogens and oral contraceptives.

Chronic alcoholism decreases the absorption of folic acid. Abstinence from alcohol will partially reverse this effect. Otherwise, it may be necessary to increase the maintenance dose.

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.

Sulfasalazine has been reported to depress folate absorption.

Prolonged use of folic acid (at high doses) decreases serum levels of cyanocobalamin.

4.6 Fertility, pregnancy and lactation

Pregnancy

Category A.

Folic acid crosses the placenta, however adequate and well controlled studies in humans have shown that therapeutically acceptable doses of folic acid may be safely administered to pregnant women.

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.

Breastfeeding

Folic acid 5-methyltetrahydrofolate and 10-formyltetrahydrofolate are excreted in 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.

Fertility

No data available.

4.7 Effects on ability to drive and use machines

FOLIC ACID VIATRIS has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Folic acid is generally well tolerated.

System	Frequency	Adverse events
Gastrointestinal disorders	Rare (≥1/10,000 to <1/1,000)	Anorexia, nausea, diarrhoea, flatulence, gastro-intestinal disturbances, abdominal distension.
Immune System disorders	Rare (≥1/10,000 to <1/1,000)	Allergic reactions, comprising erythema, rash, pruritus, urticaria, dyspnoea, bronchospasm, and anaphylactic reactions (including shock), fever.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Folic acid has a low acute and chronic toxicity profile. Adults receiving a daily dose of 400 mg for 5 months followed by a daily dose of 10 mg for 5 years did not present any adverse side effects.

There are no serious or irreversible symptoms of intoxication with oral folic acid. No specific measures are required in the event of overdose.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: folic acid and derivatives
ATC code: B03BB01

Mechanism of action

Folic acid is a member of the vitamin B group and is the substrate for the production of tetrahydrofolate by enzymatic reduction *in vivo*. Tetrahydrofolate is a coenzyme for various metabolic pathways including purine and pyrimidine nucleotide synthesis, and ultimately DNA synthesis. It is also involved in some amino acid conversions, and in the formation and utilisation of formate. It is involved in the maturation of all rapidly proliferating tissues particularly those of bone marrow and gastrointestinal tract. Folic acid deficiency develops from inadequate dietary intake through malnutrition or malabsorption or may result from increased utilisation in pregnancy or conditions such as haemolytic anaemia. Folate deficiency is also an adverse side effect of chemotherapeutic agents that function as folate antagonists by interfering with folate metabolism.

Conclusive evidence that folic acid therapy when taken as a supplement by women during the periconceptional period significantly reduces the incidence of foetal neural tube defects was established by a multinational, multicentre, controlled clinical study organised by the Medical Research Council in the United Kingdom. In the final report of this study published in 1991, investigators concluded that a daily supplement of folic acid would be beneficial to all women

planning a pregnancy. A later randomised controlled clinical study conducted in Hungary established that a daily dose of 0.8 mg folic acid was effective for reducing the incidence of neural tube defects.

5.2 Pharmacokinetic properties

Absorption

Orally administered folic acid is rapidly absorbed mainly from the wall of the proximal small intestine as the 5-methyltetrahydrofolate metabolite. This metabolite is extensively bound to plasma proteins in the portal circulation.

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

Folic acid is rapidly absorbed from normal diets, is extensively plasma bound and is widely distributed in body tissues via portal circulation with the liver as the principal storage site. it is also actively concentrated in the CSF. Folate is also distributed in 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

There is an enterohepatic circulation for folate; approximately 4 to 5 micrograms is excreted in the urine daily. Urinary levels of excreted folate are a function of dose. Folic acid is removed by haemodialysis.

5.3 Preclinical safety data

Not applicable

6. Pharmaceutical Particulars

6.1 List of excipients

FOLIC ACID VIATRIS tablet also contains

- Maize starch
- Lactose
- Crospovidone
- Povidone
- Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store at or below 30°C.

Protect from light.

6.5 Nature and contents of container

White HDPE bottle and a green polypropylene wadded screw cap. Pack-sizes of 100 tablets.

Blue HDPE bottle and a blue polypropylene induction seal screw cap. Pack-sizes of 100 tablets.

Not all pack types may be marketed.

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

Pharmacy Only Medicine

8. Sponsor Details

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Ellerslie
AUCKLAND
www.viatris.co.nz
Telephone 0800 168 169

9. Date of First Approval

15 June 2021

10. Date of Revision of the Text

22 November 2023

Summary table of changes

Section	Summary of new information
4.8	Minor editorial updates and formatting changes
2	Inclusion of excipients with potential to contain sulfites. Inclusion of allergen declaration
4.2	Addition of: monitoring and dose adjustment due to risk of relapse. Administer orally except severe disease or in severe cases of intestinal malabsorption.

	In concomitant therapy with antiepileptic drugs, the daily dose use lowest effective amount and divided into multiple single doses.
4.3	Addition of: The haematological features of vitamin B12 deficiency may be corrected with folic acid but the neurological effects will not be alleviated and may become irreversible.
4.4	Addition of: Absorption impaired by severe deficiency or server malabsorption. Vitamin B12 deficiency needs to be excluded before folic acid is prescribed. Cobalamin deficiency can go undetected for several years, during which time the neuropsychiatric manifestations may become irreversible (and worsen with folate supplementation). Hence, for elderly patients, a cobalamin absorption test should be performed prior to starting long-term folate treatment. Large doses of folic acid may counteract the anti-epileptic effect of diphenylhydantoin.
4,5	Addition of: monitor antiepileptic drug concentrations and adjust (increase) their dose accordingly. levels of folate due to antiepileptics, adjustment (increase) of maintenance dose of folic acid may be required depending on the severity of folic acid deficiency. In patients experiencing haemolytic anaemia or anticonvulsant therapy, it may be necessary to increase the maintenance dose. Methotrexate has a high affinity for mammalian dihydrofolate reductase and therefore inhibits the reduction of folic acid to tetrahydrofolate. Trimethoprim and pyrimethamine are more selective inhibitors of microbial dihydrofolate reductase, the concentrations required to inhibit the mammalian enzyme are 10,000 to 50,000 times greater than the concentrations required to inhibit the microbial enzyme for trimethoprim and 1,400 times greater for pyrimethamine. Sulfasalazine has been reported to depress folate absorption. Prolonged use of folic acid (at high doses) decreases serum levels of cyanocobalamin.
4.6	Include 5-methyltetrahydrofolate and 10-formyltetrahydrofolate for excretion in breast-feeding section
4.8	Updated reporting URL to: https://pophealth.my.site.com/carmreportnz/s/
4.9	Removal of: No reports of over dosage.

	Addition of: There are no serious or irreversible symptoms of intoxication with oral folic acid. No specific measures are required in the event of overdose
6.1	Deletion of: Sulfites may be present in this product in trace amounts. If you have been told by your doctor that you have an intolerance to some sugars and sulfites, contact your doctor before taking this medicinal product.
10	Update Date of revision of text