

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

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.

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 to 10 mg but could be much higher.

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.

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 B₁₂ 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..

4.4 Special warnings and precautions for use

Folic acid should never be administered for the treatment of undiagnosed megaloblastic anaemia including in infancy, pernicious anaemia or macrocytic anaemia of unknown aetiology or other cause of cobalamin deficiency, including lifelong vegetarian, without first excluding vitamin B₁₂ deficiency as the cause. The haematopoietic response to folic acid therapy may be misinterpreted as an improvement in the condition of vitamin B₁₂ deficient patients, but irreversible neurological lesions may develop as a consequence of masking the true deficiency state.

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. 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

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.

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.

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.

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.

Breast-feeding

Folic acid is 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 ($\geq 1/10,000$ to $< 1/1,000$)	Anorexia, nausea, diarrhoea, flatulence, gastro-intestinal disturbances
Immune System disorders	Rare ($\geq 1/10,000$ 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://nzphvc.otago.ac.nz/reporting/>.

4.9 Overdose

No reports of over dosage have been reported.

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.

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 and is widely distributed in body tissues 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

Sulfites may be present in this product in trace amounts.

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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AUCKLAND
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9. Date of First Approval

15 June 2021

10. Date of Revision of the Text

15 September 2022

Summary table of changes

Section	Summary of new information
All	Minor editorial and formatting changes
4.3	<p>Rewording for better flow.</p> <p>Addition of Long-term folate therapy being contraindicated in any patient with untreated cobalamin deficiency.</p> <p>Addition of statement for Folic acid use given alone to treat Addisonian pernicious anaemia, other vitamin B12 deficiency states as it may precipitate the onset of subacute combined degeneration of the spinal cord.</p>
4.4	<p>Addition of extra conditions when folic acid should not be administered.</p> <p>Addition of Caution when administering folic acid to patients who may have folate dependent tumours.</p> <p>Addition of statement about 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.</p> <p>Addition of statement for patients with galactose intolerance, total lactase deficiency or glucose – galactose malabsorption</p>
4.5	<p>Addition of interaction with phenytoin and to a less extent other anticonvulsants. Sulphasalazine and triamterene also inhibit absorption.</p> <p>Addition of antibacterial which interact with folate metabolism.</p> <p>Addition of Nitrous oxide anaesthesia may cause an acute folic acid deficiency.</p> <p>Addition of statements on enhancement of lithium efficacy, Folinic acid, and that ethanol and aspirin increase folic elimination.</p>
4.6	<p>Additional details added about congenital anomalies, spontaneous abortions, and intrauterine growth retardation.</p> <p>Additional information of folate accumulation in milk.</p>
4.8	Adverse event moved into table and additional events added to immune system disorders and anorexia added to gastrointestinal disorders.
5.1	More specific Pharmacotherapeutic group and ATC code identified.
5.2	Addition information added to absorption, distribution, biotransformation, elimination.

10	Update Date of revision of text
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