



## APO-FOLIC

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### 1. APO-FOLIC (0.8mg and 5mg)

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

#### Name and strength of the active substance

Folic acid 0.8mg

Folic acid 5mg

Excipient with known effect

Lactose and Gluten

Apo-Folic contain Lactose and gluten. If you have been told by your doctor that you have an intolerance to some sugars and gluten, contact your doctor before taking this medicinal product.

For a full list of excipients, see section 6.1.

### 3. PHARMACEUTICAL FORM

APO-FOLIC 0.8mg tablets are yellow, round, 5.5mm in diameter, biconvex tablets, engraved "F" over "0.8" one side and "APO" on the other side. Each tablet contains 0.8mg of folic acid and typically weighs 85mg.

APO-FOLIC 5mg tablets are yellow, round, 6.5 mm in diameter, flat with bevelled edges and engraved "F5" on one side and "APO" on the other side. Each tablet contains 5mg of folic acid and typically weighs 82mg.

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutic indications

APO-FOLIC 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.

APO-FOLIC 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.

APO-FOLIC 0.8 mg tablets are indicated as a daily supplement to be taken by women planning pregnancy to reduce the risk of neonatal conditions developing from foetal neural tube defects.

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## 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 5-10mg, 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.

### Method of administration

Folic acid should not be added to multivitamin preparations as it may lower concentration of vitamin B<sub>12</sub> in the blood.

- APO-FOLIC 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 2.5-10mg.

Children: 5-15mg 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.

- Paediatric use:

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

- APO-FOLIC 0.8 mg tablets
  - Prophylaxis of neural tube defects:

1 tablet (0.8 mg) taken daily for 4 weeks before conception and during the first trimester of pregnancy. It may be advantageous to the patient to continue this dosing schedule throughout the full term of pregnancy and during lactation for general prophylaxis of folate deficiency. APO-FOLIC 0.8 mg tablets are intended as a supplement for women of childbearing potential only.

## 4.3 Contraindications

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

Megaloblastic anaemia resulting from cyanocobalamin (Vitamin B<sub>12</sub>) deficiency should not be treated with folic acid as the neurological defects of vitamin B<sub>12</sub> deficiency will not be alleviated, and may become irreversible.

Caution is advised in patients who may have folate-dependant tumours.

#### **4.4 Special warnings and precautions for use**

Folic acid should never be administered for the treatment of undiagnosed megaloblastic anaemia 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.

#### **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.

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 carbamaepine, oestrogens and oral contraceptives.

Chronic alcoholism decreases the absorption of folic acid. Abstinence from alcohol will partially reverse this effect.

#### **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.

##### **Breast-feeding**

Folic acid is excreted in breast milk, but problems in humans have not been documented with intake of normal daily requirements.

##### **Fertility**

APO-FOLIC 0.8 mg tablets are intended as a supplement for women of childbearing potential only.

#### **4.7 Effects on ability to drive and use machines**

Presumed to be safe or unlikely to produce an effect on the ability to drive or use machinery.

#### **4.8 Undesirable effects**

Folic acid is generally well tolerated.

Although uncommon, nausea diarrhoea, flatulence and gastro-intestinal disturbances have been associated with folic acid therapy.

Hypersensitivity reactions such as bronchospasm, erythema, fever rash or itching have been reported rarely.

#### **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 advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic Properties**

Pharmacotherapeutic group: antianemic preparations

ATC code: B03BB

### **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**

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. Folic acid is rapidly absorbed from normal diets and is widely distributed in body tissues with the liver as the principal storage site. Folate is also distributed in breast milk.

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.

## **5.3 Preclinical safety data**

Not applicable

# **6. PHARMACEUTICAL PARTICULARS**

## **6.1 List of excipients**

Apo –Folic acid 0.8mg and 5mg tablet contains the following excipients:

- Wheaten Cornstarch
- PVP/VA Copolymer
- Lactose Special Dense
- Aerosil 200
- Magnesium Stearate

Apo-Folic acid 0.8mg and 5mg contain lactose and gluten.

## **6.2 Incompatibilities**

Not applicable

## **6.3 Shelf life**

0.8mg Folic acid has shelf life of 24 months from the date of manufacture  
5mg Folic acid has shelf life of 60 months from the date of manufacture

## **6.4 Special Precautions**

Store at or below 30°C

Protect from heat, light and moisture. Keep the container tightly closed.

## **6.5 Nature and contents of container**

APO-FOLIC ACID 0.8mg tablets: HDPE Bottles of 100,120, 500 and 1000 tablets

APO-FOLIC ACID 5mg tablets: HDPE Bottles of 500 tablets

## **6.6 Special precautions for disposal**

No special requirements for disposal.

Any unused medicine or waste material should be disposed of in accordance with local requirements.

## **7. MEDICINE SCHEDULE**

Pharmacy Only Medicine

## **8. SPONSOR**

Apotex NZ Ltd.  
32 Hillside Road  
Glenfield  
AUCKLAND 0627

Telephone: (09) 444 2073

Fax: (09) 444 2951

E-mail: NZcustomerservice@apotex.com

## **9. DATE OF FIRST APPROVAL**

03 December 1981- 5 mg Folic acid

20 July 1995- 0.8mg Folic acid

## **10. DATE OF REVISION OF THE TEXT**

27 February 2017

### **Summary Table of Changes**

<b>Section changed</b>	<b>Summary of new information</b>
Whole data sheet	Reformatted as per Medsafe new data sheet
6.1	Additional information as per Medsafe requirements  Apo-Folic acid contains lactose and gluten