AUSTRALIAN PRODUCT INFORMATION

MEGAFOL

(folic acid) tablets

1 NAME OF THE MEDICINE

Folic acid

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each MEGAFOL 0.5 tablet contains 0.5 mg of folic acid as the active ingredient.

Each MEGAFOL 5 tablet contains 5 mg of folic acid as the active ingredient.

Excipients with known effect: Sulfites and sugars as lactose.

For the full list of excipients, see Section 6.1 LIST OF EXCIPIENTS.

3 PHARMACEUTICAL FORM

MEGAFOL 0.5 mg: 6.5 mm, normal convex, yellow tablet with scoreline on one side and blank on the other

MEGAFOL 5 mg: 7 mm, flat bevelled edged, yellow tablet with scoreline on one side and blank on the other

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Treatment of megaloblastic anaemia due to a deficiency of folic acid; prophylaxis during pregnancy and lactation.

4.2 DOSE AND METHOD OF ADMINISTRATION

Prophylaxis during pregnancy and lactation.

0.5 mg daily, taken orally.

Treatment of megaloblastic anaemia.

1 to 5 mg daily, taken orally, according to the severity of anaemia and the presence/absence of malabsorption syndromes.

4.3 CONTRAINDICATIONS

Avoid treating megaloblastic anaemia due to vitamin B12 deficiency with folic acid. 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 (see Section 4.3 CONTRAINDICATIONS).

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

Folic acid does not correct folate deficiency due to dihydrofolate reductase inhibitors (see Section 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS).

Folinic acid should be used for this purpose.

Use in the Elderly

Cobalamin deficiency can go undiagnosed for an extended duration, during which the neuropsychiatric manifestations may become irreversible (and may be aggravated by folate supplementation).

Paediatric Use

No data available.

Effects on Laboratory Tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Alcoholism and anticonvulsant therapy can cause folate deficiency. In patients experiencing chronic haemolytic anaemia, daily supplementation of folic acid can lead to a marked increase in serum folate levels.

Folic acid supplementation may decrease serum antiepileptic concentrations in patients receiving anticonvulsant therapy, leading to decreased seizure control. Serum folate and antiepileptic concentrations should be monitored in patients receiving concomitant treatment as dosage adjustment for both treatment regimens may be required.

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.

High intravenous doses of folic acid with concomitant administration of fluorouracil can cause severe diarrhoea.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on Fertility

No data available.

Use in Pregnancy

Pregnancy Category: A

Use in Lactation

Folic acid, 5-methyltetrahydrofolate and 10-formyltetrahydrofolate are excreted in breast milk. Therapeutic indications include supplementation in lactating or pregnant women when they are folic acid deficient.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

Folic acid is usually well tolerated in humans; however, gastrointestinal disturbances and CNS effects have occasionally been reported following high doses (incidence of less than 1% at dose of 15 mg/day), and isolated reports of allergic sensitivity reactions including bronchospasm and rash have been documented.

Reporting Suspected Adverse Effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Folic acid is reduced in the body to a number of compounds including tetrahydrofolic acid. In the reduced form, it acts as a coenzyme for various metabolic processes. It is necessary for the synthesis of purine and pyrimidine nucleotides and hence DNA synthesis, and is involved in some amino acid conversions. The maturation of all rapidly proliferating tissues, in particular the bone marrow and the gastrointestinal tract, require folic acid. Folate deficiency leads to megaloblastic anaemia.

Mechanism of Action

Treatment of folic acid deficiency. Folic acid deficiency is defined by WHO as serum folate levels below 3ng/mL or red cell folate levels below 100 ng/mL. Deficiency may be due to inadequate dietary intake, malabsorption, or increased utilisation of folic acid. Dietary intake may be inadequate in infants fed solely on goat's milk or when diet is poor, particularly when it is low in vegetable constituents. Folates in food are largely present in the form of polyglutamates which are hydrolysed enzymatically at the gastrointestinal mucosa to folic acid. Conditions in which folate utilisation is increased include: pregnancy and lactation; haemolytic anaemia; hyperthyroidism; exfoliative dermatitis; and chronic infection.

Clinical Trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Folic acid is absorbed from the upper gastrointestinal tract. It is generally well absorbed; however, absorption is decreased in chronic alcoholics, in malabsorptive diseases such as tropical and coeliac sprue, in patients with systemic bacterial infection, in patients receiving diphenylhydantoin, and following procedures such as gastrectomy and upper intestinal resection.

Distribution

It is stored in tissues, especially the liver, predominantly as methylated polyglutamates. 5-methyltetrahydrofolate is also secreted in bile. Enterohepatic recycling of folate may provide as much as

200 μg or more folate each day for recirculation to the tissues. Folic acid and 5-methyltetrahydrofolate cross the placenta and accumulate in the foetal liver.

5-methyltetrahydrofolate is also actively transported into the cerebrospinal fluid.

Metabolism

Folic acid is rapidly metabolised primarily to 5-methyltetrahydrofolate with some 10-formylfolate and some 10-formyltetrahydrofolate formed.

Excretion

Folic acid is excreted in urine unchanged and as a number of metabolites (including 5-methyltetrahydrofolate and pterins). Folic acid is also excreted in faeces.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

MEGAFOL contains the following excipients: Crospovidone, lactose, maize starch, povidone, magnesium stearate.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 30°C.

6.5 NATURE AND CONTENTS OF CONTAINER

Container type: HDPE Bottles

Pack sizes: 30, 100, 1000

Australian Register of Therapeutic Goods (ARTG)

AUST R 17706 – MEGAFOL 5 folic acid 5 mg tablet bottle

AUST R 27951 – MEGAFOL 0.5 folic acid 0.5 mg tablet bottle

Some strengths, pack sizes and/or pack types may not be marketed.

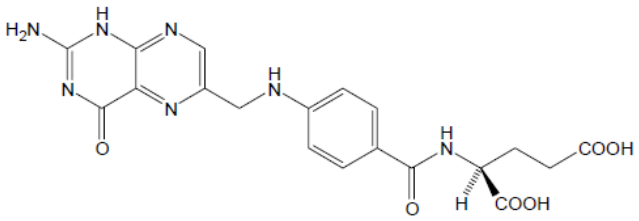
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking it to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Yellow to orange, crystalline powder; odourless or almost odourless. Practically insoluble in cold water, ethanol, and most organic solvents. Soluble in dilute acids and in alkaline solutions, and boiling water (to 1 g/100 mL). Chemically, it is pteroylglutamic acid, N-[4-[[(2-amino-1,4-dihydro-4-oxo-6-pteridinyl)methyl] amino]benzoyl]-L-glutamic acid. The chemical structure is shown below.

Chemical Structure



Chemical name: (2S)-2-[[4-[(2-Amino-4-oxo-1H-pteridin-6-yl)methylamino]benzoyl]amino]pentanedioic acid

Molecular weight: 441.4

Molecular Formula: $C_{19}H_{19}N_7O_6$

CAS Number:

59-30-3

7 MEDICINE SCHEDULE (POISONS STANDARD)

0.5 mg: Unscheduled

5 mg: S2 (Pharmacy Medicine)

8 SPONSOR

Alphapharm Pty Ltd trading as Viatris

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Millers Point NSW 2000

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Phone: 1800 274 276

9 DATE OF FIRST APPROVAL

20/09/1991

10 DATE OF REVISION

11/11/2024

Summary Table of Changes

Section Changed	Summary of New Information
4.2	Method of administration added i.e., 'taken orally'.
4.4	Addition of information regarding absorption in cases of severe deficiency and severe intestinal malabsorption. Addition of information regarding Cobalamin deficiency.
4.5	Information included for patients experiencing alcoholism, hemolytic anaemia or anticonvulsant therapy. Addition of interaction with antiepileptic drugs and flouracil. Information included regarding prolonged use.

Megafol_pi\Nov24/01 (CCDS 07-Sep-2023)