FOLIC ACID INJECTION 5 MG IN 1 ML

(FOLIC ACID)

1 NAME OF THE MEDICINE

Folic acid

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Folic Acid Injection contains 5 mg of folic acid in water for injections to 1 mL.

Folic acid is a complex organic compound present in liver, yeast and natural sources. It also may be prepared synthetically. The pH range is 8.0-11.0.

For the full list of excipients, see Section 6.1 List of Excipients.

3 PHARMACEUTICAL FORM

Folic Acid Injection is a sterile solution. It is presented as 1 mL of solution in a 2 mL glass vial.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Folic Acid Injection is indicated for the treatment of megaloblastic anaemia, where this has been shown to be due to folic acid deficiency either due to inadequate dietary intake, malabsorption or increased utilisation, including pregnancy and lactation, haemolytic anaemia, hyperthyroidism, exfoliative dermatitis and chronic infection. It is also indicated for prophylaxis during pregnancy and lactation.

4.2 DOSE AND METHOD OF ADMINISTRATION

Folic Acid Injection is used for parenteral folic acid therapy, and may be administered, usually by intramuscular, or less commonly by intravenous or subcutaneous injection.

A dilute solution of folic acid containing 100 micrograms/mL may be prepared by adding 1 mL (5 mg of folic acid) of the injection to 49 mL of sterile water for injection.

For treatment of megaloblastic anaemia in adults, 1 to 5 mg/day is recommended. Adjust the dosage according to the severity of the anaemia and to the presence or absence of malabsorption syndromes. For the treatment of megaloblastic anaemia in preterm infants less than 2 kg body weight, 100 to 200 micrograms daily, orally or intramuscularly, should be used. Treating megaloblastic anaemia in infants of 5-12 months of age, a satisfactory response has been obtained using 50 micrograms daily, orally or intramuscularly.

The usual therapeutic dose in paediatric practice for the treatment of megaloblastic anaemia due to folic acid deficiency is 1 to 5 mg daily. This supra-physiological dosage can produce a partial haematological response in primary B_{12} deficiency and therefore must not be used until B_{12} deficiency has been excluded.

For prophylaxis in pregnancy and lactation, 500 micrograms folic acid / day prevented signs of folic acid deficiency in well-nourished pregnant women.

Folic Acid Injection should be used in one patient on one occasion only. It contains no anti-microbial preservative. Unused solution should be discarded.

4.3 CONTRAINDICATIONS

Folic Acid Injection is contraindicated in patients who may be hypersensitive to it. Although rare, an anaphylactic reaction has been reported. Folic Acid Injection should not be prescribed for megaloblastic anaemia due to vitamin B_{12} deficiency.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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

Folic acid treatment may correct the haematological features of vitamin B_{12} deficiency without correcting the progressive neurological damage due to vitamin B_{12} deficiency. Therefore, vitamin B_{12} deficiency needs to be excluded before treatment with folic acid alone.

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, such as methotrexate. Folinic acid should be used for this purpose.

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

Use in the elderly

No data available.

Paediatric use

See Section 4.2 Dose and Method of Administration.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Folic acid affects the disposition of anticonvulsants. 15 mg of folic acid given intramuscularly decreased total serum diphenylhydantoin concentration by 15% without altering its unbound concentration, by increasing the urinary excretion of metahydroxy-diphenylhydantoin and diphenylhydantoin. A decrease in the steady state plasma concentration and a decrease in the half life for phenobarbitone have been reported following 30 mg of folic acid daily for 3 months in folate deficient epileptics.

Dihydrofolate reductase inhibitors such as methotrexate, trimethoprim and pyrimethamine prevent the reduction of folic acid to tetrahydrofolate.

Sulphasalazine has been reported to depress folic acid absorption.

Absorption of folic acid is decreased in chronic alcoholics. This effect can be partially reversed by abstinence from alcohol.

See Section 6.2 Incompatibilities.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy

Folic Acid Injection is pregnancy Category A - Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.

Therapeutic indications include used for prophylaxis during pregnancy and supplementation of lactating women when they are folic acid deficient.

Use in lactation

Folic acid is excreted in breast milk.

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 Injection appears to be well tolerated, however nausea, flatulence, diarrhoea, irritability and sleep disturbances have been reported uncommonly (with 5 mg/day) along with isolated reports of rash and bronchospasm. EEG changes and convulsion have been reported with intravenous therapy. Although rare, an anaphylactic reaction has been reported.

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 http://www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

In a double blind randomised trial, 15 mg of folic acid per day for one month produced no signs of toxicity in healthy volunteers.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

Folic acid is reduced to a number of compounds including tetrahydrofolic acid in the body. In the reduced form it is a coenzyme acting as an acceptor of one-carbon units. It is required for the synthesis of purine and pyrimidine bases, for the metabolism of amino acids such as serine-glycine interconversion, methionine methyl group

biosynthesis and the degradation of histidine. It is involved in the maturation of all rapidly proliferating tissues particularly those of bone marrow and gastrointestinal tract. Folate deficiency leads to megaloblastic anaemia.

Clinical trials

No data available.

5.2 PHARMACOKINETIC PROPERTIES

Absorption

Folic acid is absorbed mainly from the proximal part of the small intestine. The naturally occurring folate polyglutamates are largely deconjugated and reduced prior to absorption. It is the 5-methyltetrahydrofolate which appears in the portal circulation, where it is extensively bound to plasma proteins.

Distribution

Folic acid is rapidly absorbed from normal diets and is distributed in body tissues. The principal storage site is the liver. Folate is distributed into breast milk.

Metabolism

No data available.

Excretion

There is an enterohepatic circulation for folate; about 4 to 5 micrograms is excreted in the urine daily. Administration of larger doses of folic acid leads to proportionately more of the vitamin being excreted in the urine.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Folic Acid Injection contains 5mg of folic acid, sodium hydroxide and hydrochloric acid for pH adjustment in water for injections to 1mL.

The sodium content is approximately 34.5 mg/mL.

6.2 INCOMPATIBILITIES

Folic acid is incompatible with oxidising and reducing agents and with ions of heavy metals.

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)[1]. The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Protect from light.

6.5 NATURE AND CONTENTS OF CONTAINER

It is presented as 1 mL of solution in a 2 mL glass vial.

It is supplied in a carton containing 10 vials.

Phebra product code - INJ085

The vial stopper is not made with natural rubber latex.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

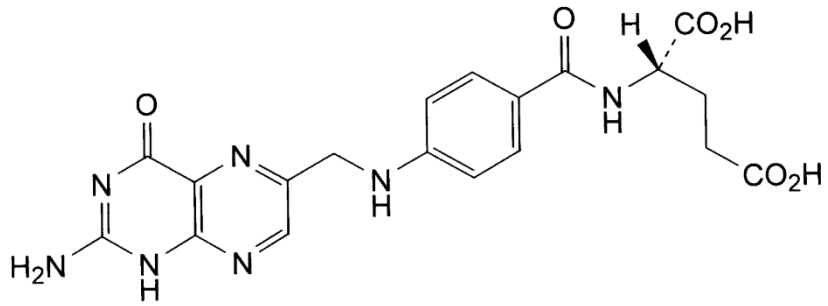
In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical name: (2S)-2-[[4-[[(2-amino-4-oxo-1,4-dihydropteridin-6-yl)methyl]amino]benzoyl]amino]pentanedioic acid.

The molecular weight of the compound is 441.4. The molecular formula is $C_{19}H_{19}N_7O_6$.

Chemical structure



CAS number

59-30-3

7 MEDICINE SCHEDULE (POISONS STANDARD)

Schedule 4 – Prescription Only Medicine.

8 SPONSOR

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9 DATE OF FIRST APPROVAL

Oct 1991

10 DATE OF REVISION

23 March 2020

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
NA	PI reformatted to align with new format.
6.5	Addition of latex statement.
8	Minor editorial update.

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