

FOLIC ACID- folic acid tablet
ECI PHARMACEUTICALS LLC

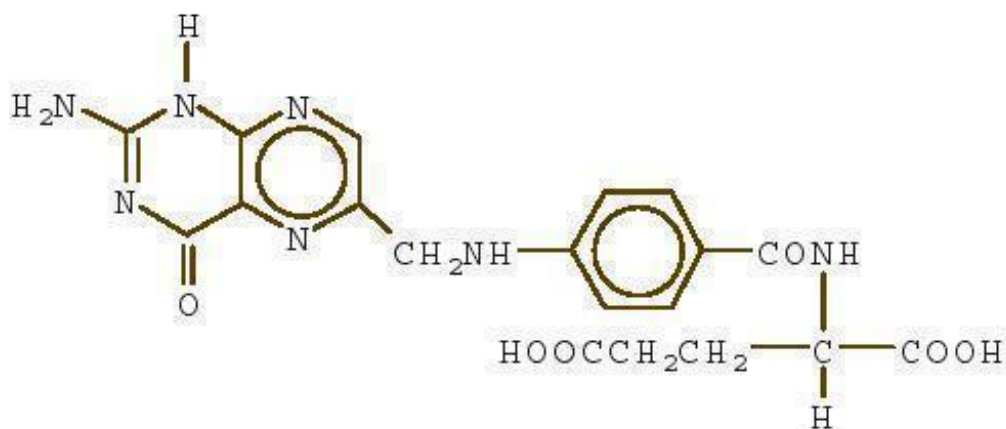
FOLIC ACID TABLETS, USP

Rx Only

DESCRIPTION

Folic acid, N-[*p*-[[(2-amino-4-hydroxy-6-pteridiny) methyl]-amino]benzoyl]-L-glutamic acid, is a B complex vitamin containing a pteridine moiety linked by a methylene bridge to para-aminobenzoic acid, which is joined by a peptide linkage to glutamic acid. Conjugates of folic acid are present in a wide variety of foods, particularly liver, kidneys, yeast, and leafy green vegetables. Commercially available folic acid is prepared synthetically. Folic acid occurs as a yellow or yellowish-orange crystalline powder and is very slightly soluble in water and insoluble in alcohol. Folic acid is readily soluble in dilute solutions of alkali hydroxides and carbonates, and solutions of the drug may be prepared with the aid of sodium hydroxide or sodium carbonate, thereby forming the soluble sodium salt of folic acid (sodium folate). Aqueous solutions of folic acid are heat sensitive and rapidly decompose in the presence of light and/or riboflavin; solutions should be stored in a cool place protected from light.

The structural formula of folic acid is as follows:



Each tablet, for oral administration, contains 1 mg folic acid.

Folic Acid Tablets, USP 1 mg contain the following inactive ingredients: lactose monohydrate, microcrystalline cellulose, sodium starch glycolate and magnesium stearate.

CLINICAL PHARMACOLOGY

Folic acid acts on megaloblastic bone marrow to produce a normoblastic marrow.

In man, an exogenous source of folate is required for nucleoprotein synthesis and the maintenance of normal erythropoiesis. Folic acid is the precursor of tetrahydrofolic acid, which is involved as a cofactor for transformylation reactions in the biosynthesis of purines and thymidylates of nucleic acids. Impairment of thymidylate synthesis in

patients with folic acid deficiency is thought to account for the defective deoxyribonucleic acid (DNA) synthesis that leads to megaloblast formation and megaloblastic and macrocytic anemias.

Folic acid is absorbed rapidly from the small intestine, primarily from the proximal portion. Naturally occurring conjugated folates are reduced enzymatically to folic acid in the gastrointestinal tract prior to absorption. Folic acid appears in the plasma approximately 15 to 30 minutes after an oral dose; peak levels are generally reached within 1 hour. After intravenous administration, the drug is rapidly cleared from the plasma. Cerebrospinal fluid levels of folic acid are several times greater than serum levels of the drug. Folic acid is metabolized in the liver to 7,8-dihydrofolic acid and eventually to 5,6,7,8-tetrahydrofolic acid with the aid of reduced diphosphopyridine nucleotide (DPNH) and folate reductases. Tetrahydrofolic acid is linked in the N⁵ or N¹⁰ positions with formyl, hydroxymethyl, methyl, or formimino groups. N⁵-formyltetrahydrofolic acid is leucovorin. Tetrahydrofolic acid derivatives are distributed to all body tissues but are stored primarily in the liver. Normal serum levels of total folate have been reported to be 5 to 15 ng/mL; normal cerebro-spinal fluid levels are approximately 16 to 21 ng/mL. Normal erythrocyte folate levels have been reported to range from 175 to 316 ng/mL. In general, folate serum levels below 5 ng/mL indicate folate deficiency, and levels below 2 ng/mL usually result in megaloblastic anemia.

After a single oral dose of 100 µg of folic acid in a limited number of normal adults, only a trace amount of the drug appeared in the urine. An oral dose of 5 mg in 1 study and a dose of 40 µg/kg of body weight in another study resulted in approximately 50% of the dose appearing in the urine. After a single oral dose of 15 mg, up to 90% of the dose was recovered in the urine. A majority of the metabolic products appeared in the urine after 6 hours; excretion was generally complete within 24 hours. Small amounts of orally administered folic acid have also been recovered in the feces. Folic acid is also excreted in the milk of lactating mothers.

INDICATIONS AND USAGE

Folic acid is effective in the treatment of megaloblastic anemias due to a deficiency of folic acid (as may be seen in tropical or nontropical sprue) and in anemias of nutritional origin, pregnancy, infancy, or childhood.

CONTRAINDICATIONS

Folic acid is contraindicated in patients who have shown previous intolerance to the drug.

WARNING

Administration of folic acid alone is improper therapy for pernicious anemia and other megaloblastic anemias in which vitamin B₁₂ is deficient.

PRECAUTIONS

General

Folic acid in doses above 0.1 mg daily may obscure pernicious anemia in that hematologic remission can occur while neurologic manifestations remain progressive.

There is a potential danger in administering folic acid to patients with undiagnosed anemia, since folic acid may obscure the diagnosis of pernicious anemia by alleviating the hematologic manifestations of the disease while allowing the neurologic complications to progress. This may result in severe nervous system damage before the correct diagnosis is made. Adequate doses of vitamin B₁₂ may prevent, halt, or improve the neurologic changes caused by pernicious anemia.

Drug Interactions

There is evidence that the anticonvulsant action of phenytoin is antagonized by folic acid. A patient whose epilepsy is completely controlled by phenytoin may require increased doses to prevent convulsions if folic acid is given.

Folate deficiency may result from increased loss of folate, as in renal dialysis and/or interference with metabolism (e.g., folic acid antagonists such as methotrexate); the administration of anticonvulsants, such as diphenylhydantoin, primidone, and barbiturates; alcohol consumption and, especially, alcoholic cirrhosis; and the administration of pyrimethamine and nitrofurantoin.

False low serum and red cell folate levels may occur if the patient has been taking antibiotics, such as tetracycline, which suppress the growth of *Lactobacillus casei*.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential and studies to evaluate the mutagenic potential or effect on fertility have not been conducted.

Pregnancy

Teratogenic Effects

Pregnancy Category A

Folic acid is usually indicated in the treatment of megaloblastic anemias of pregnancy. Folic acid requirements are markedly increased during pregnancy, and deficiency will result in fetal damage (see **INDICATIONS AND USAGE**).

Studies in pregnant women have not shown that folic acid increases the risk of fetal abnormalities if administered during pregnancy. If the drug is used during pregnancy, the possibility of fetal harm appears remote. Because studies cannot rule out the possibility of harm, however, folic acid should be used during pregnancy only if clearly needed.

Nursing Mothers

Folic acid is excreted in the milk of lactating mothers. During lactation, folic acid requirements are markedly increased; however, amounts present in human milk are adequate to fulfill infant requirements, although supplementation may be needed in low-birth-weight infants, in those who are breast-fed by mothers with folic acid deficiency (50 µg daily), or in those with infections or prolonged diarrhea.

ADVERSE REACTIONS

Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

Folic acid is relatively nontoxic in man. Rare instances of allergic responses to folic acid preparations have been reported and have included erythema, skin rash, itching, general malaise, and respiratory difficulty due to bronchospasm. One patient experienced symptoms suggesting anaphylaxis following injection of the drug. Gastrointestinal side effects, including anorexia, nausea, abdominal distention, flatulence, and a bitter or bad taste, have been reported in patients receiving 15 mg folic acid daily for 1 month. Other side effects reported in patients receiving 15 mg daily include altered sleep patterns, difficulty in concentrating, irritability, overactivity, excitement, mental depression, confusion, and impaired judgment. Decreased vitamin B₁₂ serum levels may occur in patients receiving prolonged folic acid therapy.

In an uncontrolled study, orally administered folic acid was reported to increase the incidence of seizures in some epileptic patients receiving phenobarbital, primidone, or diphenylhydantoin. Another investigator reported decreased diphenylhydantoin serum levels in folate-deficient patients receiving diphenylhydantoin who were treated with 5 mg or 15 mg of folic acid daily.

OVERDOSAGE

Except during pregnancy and lactation, folic acid should not be given in therapeutic doses greater than 0.4 mg daily until pernicious anemia has been ruled out. Patients with pernicious anemia receiving more than 0.4 mg of folic acid daily who are inadequately treated with vitamin B₁₂ may show reversion of the hematologic parameters to normal, but neurologic manifestations due to vitamin B₁₂ deficiency will progress. Doses of folic acid exceeding the Recommended Dietary Allowance (RDA) should not be included in multivitamin preparations; if therapeutic amounts are necessary, folic acid should be given separately.

DOSAGE AND ADMINISTRATION

Oral administration is preferred. Although most patients with malabsorption cannot absorb food folates, they are able to absorb folic acid given orally. Parenteral administration is not advocated but may be necessary in some individuals (e.g., patients receiving parenteral or enteral alimentation). Doses greater than 0.1 mg should not be used unless anemia due to vitamin B₁₂ deficiency has been ruled out or is being adequately treated with a cobalamin. Daily doses greater than 1 mg do not enhance the hematologic effect, and most of the excess is excreted unchanged in the urine.

The usual therapeutic dosage in adults and children (regardless of age) is up to 1 mg daily. Resistant cases may require larger doses.

When clinical symptoms have subsided and the blood picture has become normal, a daily maintenance level should be used, i.e., 0.1 mg for infants and up to 0.3 mg for children under 4 years of age, 0.4 mg for adults and children 4 or more years of age, and 0.8 mg for pregnant and lactating women, but never less than 0.1 mg/day. Patients should be kept under close supervision and adjustment of the maintenance level made if relapse appears imminent.

In the presence of alcoholism, hemolytic anemia, anticonvulsant therapy, or chronic infection, the maintenance level may need to be increased.

HOW SUPPLIED

Folic Acid Tablets, USP 1 mg are yellow, scored, round, standard convex debossed with "B", "—" and "01" on one side and plain on the other side supplied in bottles of 100 and 1000.

100s **NDC** 51293-846-01

1000s **NDC** 51293-846-10

Dispense in well-closed container with child-resistant closure.

Store at 20°-25°C (68°-77°F). [See USP controlled room temperature.]

Manufactured for:

ECI Pharmaceuticals, LLC

Ft. Lauderdale, FL 33309

By:

ANSHI PHARMACEUTICAL (ZHONGSHAN) INC.

Zhongshan, Guangdong 528437 P. R. China

PACKAGE LABEL.PRINCIPAL DISPLAY PANEL

The image shows the principal display panel of a package label for Folic Acid Tablets, USP 1 mg. The label is rectangular with rounded corners and a light green border. On the left side, there is a barcode with the numbers 3, 51293, 84601, and 2. To the right of the barcode, the text reads: NDC 51293-846-01, ECI Pharmaceuticals (with a green logo), Folic Acid Tablets, USP, 1 mg (in a dark red box), Rx only, and 100 TABLETS. Below the barcode, the text reads: LB8038 R0321. On the right side of the label, there is a grey rectangular area. The text on the right side of the label reads: Each tablet contains: Folic Acid, USP 1mg; Dosage: See package insert for dosage and full prescribing information.; Dispense in a well-closed container with child-resistant closure.; Store at 20°-25°C (68°-77°F). [See USP controlled room temperature.]; Tablet debossed B-01.; Mfg for: ECI Pharmaceuticals, LLC Ft. Lauderdale, FL 33309; Mfg by: Anshi Pharmaceutical (Zhongshan) Inc., China.

NDC 51293-846-01

ECI Pharmaceuticals

Folic Acid Tablets, USP

1 mg

Rx only

100 TABLETS

3
51293
84601
2

GTIN 00351293846012

LB8038 R0321

Each tablet contains:
Folic Acid, USP 1mg

Dosage: See package insert for dosage and full prescribing information.

Dispense in a well-closed container with child-resistant closure.

Store at 20°-25°C (68°-77°F). [See USP controlled room temperature.]

Tablet debossed B-01.

Mfg for: **ECI Pharmaceuticals, LLC**
Ft. Lauderdale, FL 33309
Mfg by: Anshi Pharmaceutical (Zhongshan) Inc., China

NDC: 51293-846-10



Folic Acid Tablets, USP

1 mg

Rx only
1,000 TABLETS

LB8039 R0321

Each tablet contains:
Folic Acid, USP 1mg

Dosage: See package insert for dosage and full prescribing information.

Dispense in a well-closed container with child-resistant closure.

Store at 20°-25°C (68°-77°F). [See USP controlled room temperature.]

Tablet debossed B-01.

Mfg for: **ECI Pharmaceuticals, LLC**
Ft. Lauderdale, FL 33309
Mfg by: Anshi Pharmaceutical
(Zhongshan) Inc., China

FOLIC ACID

folic acid tablet

Product Information

Product Type	HUMAN PRESCRIPTION DRUG	Item Code (Source)	NDC:51293-846
Route of Administration	ORAL		

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
FOLIC ACID (UNII: 935E97BOY8) (FOLIC ACID - UNII:935E97BOY8)	FOLIC ACID	1 mg

Inactive Ingredients

Ingredient Name	Strength
LACTOSE MONOHYDRATE (UNII: EWQ57Q8I5X)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
SODIUM STARCH GLYCOLATE TYPE A POTATO (UNII: 5856J3G2A2)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	

Product Characteristics

Color	yellow	Score	2 pieces
Shape	ROUND (convex)	Size	8mm
Flavor		Imprint Code	B;01
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:51293-846-01	100 in 1 BOTTLE; Type 0: Not a Combination Product	04/12/2021	
2	NDC:51293-846-10	1000 in 1 BOTTLE; Type 0: Not a Combination Product	04/12/2021	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA091145	04/12/2021	

Labeler - ECI PHARMACEUTICALS LLC (962476029)

Establishment

Name	Address	ID/FEI	Business Operations
Anshi Pharmaceutical (Zhongshan) Inc.		528101821	manufacture(51293-846)

Revised: 4/2021

ECI PHARMACEUTICALS LLC