PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Pr] SANDOZ® FOLIC ACID

Folic acid tablets USP

Tablets, 5 mg, Oral

USP

ATC code: B03BB01

Anemia Therapy

Sandoz Canada Inc.
110 Rue de Lauzon
Boucherville, Quebec
J4B 1E6

Initial Authorization:
November 27, 2006

Date of Revision:
November 18, 2022

Submission Control Number: 265016

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PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

Sandoz Folic Acid (folic acid) is indicated for:

- The prevention and treatment of folate deficiency due to inadequate dietary intake, absorption or utilization or increased excretion or need as in tropical sprue (not in all forms of sprue), chronic haemodialysis, chronic haemolytic anaemia, nutritional megaloblastic anaemia, megaloblastic anaemia of pregnancy, infancy, and childhood, and megaloblastic anaemia associated with primary liver disease, alcoholism with cirrhosis, or associated with anticonvulsant therapy.
- Women who are planning pregnancy or are pregnant and have had a previous pregnancy affected by a neural tube defect (NTD), who have a family history of neural tube defects, have diabetes or malabsorption disorders, who are taking folic acid antagonists or anticonvulsant drugs.

Sandoz Folic Acid should only be used in conditions in which folate deficiency has been confirmed; specific indicators are:

- the low serum or plasma folate levels [initial],
- red cell folate level [cannot distinguish between folate deficiency and cobalamin deficiency and it remains unaffected by sudden changes in folate intake since it reflects the folate status over the lifespan of a red blood cell [120 days]
- an increase in homocysteine level [often precedes the decrease in the serum folate levels but its less specific indicator.

Folic acid is not effective in reversing the effects of folic acid reductase inhibitors such as methotrexate, for which leucovorin calcium (folinic acid) must be used. However, folic acid is used during long term, low dose methotrexate therapy to prevent methotrexate toxicity, particularly oral ulceration and gastrointestinal irritation, to treat or prevent folate deficiency and to prevent hyperhomocysteinemia.

Taking this medication does not eliminate the need for a balanced nutrition.

1.1 Pediatrics

Pediatrics (<18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of Sandoz Folic Acid in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use. See 4.2 Recommended Dose and Dosage Adjustment.

For infants with documented folic acid deficiency, a more suitable formulation should be used.

1.2 Geriatrics

Geriatrics: Evidence from post-market experience suggests that use in the geriatric population is associated with differences in safety or effectiveness.

2 CONTRAINDICATIONS

Sandoz Folic Acid (folic acid) is contraindicated in:

- Patients with hypersensitivity to folic acid products and/or any of the inactive ingredients present in the drug product, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.
- People who have diseases of the small intestine, especially Crohn's disease and Sprue, may have trouble absorbing folic acid.

In the following situation, Sandoz Folic Acid should not be used because the risk outweighs any potential therapeutic benefit:

- in any patient with untreated cobalamin deficiency (evidence suggests that long term folate therapy in these subjects precipitates cobalamin neuropathy and/or the degeneration of the spinal cord).

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- Cobalamin deficiency should be ruled out before initiating treatment. High serum folate levels in individuals with low cobalamin have been associated with anemia and cognitive impairment in older individuals, an increased risk of diabetes mellitus in the offspring of pregnant women, and high levels of the cobalamin-dependent metabolites methylmalonic acid (MMA) and homocysteine. Additionally, folate supplementation in the setting of cobalamin deficiency may also impair fetal growth and brain development.
- Folic acid should not be used alone in undiagnosed megaloblastic anaemia including in infancy, pernicious anaemia or macrocytic anaemia of unknown etiology, unless administered with adequate amounts of cobalamin.
- For the prevention of neural tube defects for woman planning a pregnancy and known to be at risk (red blood cell folate concentrations below 906 nmol/L—the threshold associated with increased NTD prevalence).

4.2 Recommended Dose and Dosage Adjustment

To prevent deficiency: Adequate dietary intake of folic acid is preferred over supplementation whenever possible.

Adults (including the elderly)

In folate deficient megaloblastic anaemia: 5 mg daily for 4 months; up to 15 mg daily may be necessary for malabsorption states.

In drug induced folate deficiency: 5 mg daily for 4 months; up to 15 mg daily may be necessary for malabsorption states.

For prophylaxis in chronic haemolytic states or in renal dialysis: 5 mg every 1 to 7 days depending on underlying disease.

Prevention of neural tube defects in women known to be at risk: 5 mg daily started before conception and continued throughout the first trimester.

In sickle cell disease: 1 to 5 mg of folic acid daily

Pregnancy:

In established folate deficiency: 5 mg daily continued to term.

Higher doses have been recommended for the treatment of tropical sprue: 3 to 15 mg daily.

Pediatrics

For young children a more suitable dosage form should be used.

In folate deficient megaloblastic anaemia:

Child 1-18 years 5 mg daily for 4 months; maintenance 5 mg every 1-7 days.

In haemolytic anaemia; metabolic disorders:

Child 1-12 years 2.5 mg-5 mg once daily.

Child 12-18 years 5-10 mg once daily.

Prophylaxis of folate deficiency in renal dialysis:

Child 1-12 years 250 microgram/kg (max 10 mg) once daily.

Children 12-18 years 5-10 mg once daily.

Geriatrics

High MMA and homocysteine levels are more common in elderly adults even when serum cobalamin levels are normal, and higher doses of cobalamin supplements are required to correct MMA levels in older individuals.

Advanced age is a risk factor for folate-associated functional cobalamin Deficiency since vitamin B deficiency is a lot more common among the elderly population. A prospective survey of older adult North Americans (>60 years) revealed that 1.9% of the population had unrecognized and untreated pernicious anemia.

Prophylaxis of Neural Tube Defects (NTD): Women with a history of pregnancy complicated by NTD are considered at high risk for recurrence and are advised to take 5 mg folic acid daily

under physician supervision while not using reliable birth control (or 3 months prior to conception), continuing for 10 to 12 weeks after the last menstrual period. Thereafter, supplementation with 0.4 mg to 1 mg daily throughout pregnancy and 4 to 6 weeks postpartum or as long as breastfeeding continues is recommended. High doses (5 mg/ day) should not be made up from taking multivitamins/ supplements because of the risk of intake of harmful amounts of other components such as retinol and vitamin D.

Excessive intake of folate may obscure and potentially delay the diagnosis of vitamin B_{12} deficiency; which could translate into delayed diagnosis and can result in an increased risk of progressive, unrecognized neurological damage.

Some women with no previous history of NTD-affected pregnancy may be at increased risk due to a 1st degree relative (child, sibling or parent) with NTD, belonging to a high-risk group (e.g., Celtic, northern Chinese, Sikh heritage), or certain medical conditions (e.g., type I diabetes, therapy with valproic acid or carbamazepine, BMI >35 kg/m^2, malabsorption disorders). Such women should consider taking folic acid 5 mg daily under physician supervision when not using reliable birth control (or 3 months prior to conception), continuing until 10 to 12 weeks after the last menstrual period.

Prevention of methotrexate toxicity: See 1 INDICATIONS: 0.4 to 1 mg daily.

4.4 Administration

Do not use if seal is broken.

4.5 Missed Dose

Women should not take more than the prescribed daily dose. If a dose is missed, for one or more days, do not try to 'catch up' by taking the missed dose(s) all at one time.

5 OVERDOSAGE

Symptoms of overdosage

Following chronic administration of very high doses (over 15 mg folic acid daily for more than 4 weeks), overdosage with folic acid manifests in the form of the following symptoms: bitter taste, loss of appetite, nausea, flatulence, nightmares, agitation, depression. The incidence and intensity of epileptic attacks may increase in patients receiving antiepileptic therapy (especially with Phenobarbital, phenytoin or primidone).

Management of overdosage

No specific measures are necessary.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
oral	Tablet 5 mg of folic acid	colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, magnesium trisilicate, microcrystalline cellulose, pregelatinized starch

Available as a compressed tablet in 1000's in a High Density Polyethylene bottle with induction seal for protection.

7 WARNINGS AND PRECAUTIONS

General

Megavitamin therapy is a cause of vitamin toxicity (hypervitaminosis) for folic acid (folate).

Folic acid is not effective in the rescue treatment or overdosage of folic acid antagonists such as methotrexate.

When cholestyramine and folic acid are administered together, there may be a reduction or delay in the folic acid absorption. If concomitant therapy is required, folic acid should be administered at least 1 hour before and 4 hours after cholestyramine.

Avoid supplements containing herbs and various other non-medicinal ingredients.

Large amounts of folate can correct the megaloblastic anemia, but not the neurological damage, that can result from vitamin B_{12} deficiency. Some experts have therefore been concerned that high intakes of folate supplements might "mask" vitamin B_{12} deficiency until its neurological consequences become irreversible.

Concerns have also been raised that high folic acid intakes might accelerate the progression of preneoplastic lesions, increasing the risk of colorectal and possibly other cancers in certain individuals.

Studies have found unmetabolized folic acid in blood from children, adolescents, and adults; breastmilk; and cord blood from newborns. Limited research suggests that single doses of 300 mcg or 400 mcg folic acid (a common amount in folic acid-containing supplements or servings of fortified foods, such as breakfast cereals) result in detectable serum levels of unmetabolized folic acid, whereas doses of 100 mcg or 200 mcg do not. In addition, a dose-frequency interaction appears to occur in which smaller amounts of folic acid consumed more frequently produce higher unmetabolized folic acid concentrations than the same total dose consumed in larger, less frequent amounts.

Hematologic

Use only as an adjunct to treatment with vitamin B_{12} whenever pernicious anemia is present or suspected. However, proper diagnosis of the condition of the patient and evaluation of the underlying etiology of the deficiency state is required. The use of folic acid in pernicious anemia patients without adequate vitamin B_{12} therapy may result in hematological improvement, while neurologic manifestations continue to progress.

Food-Bound Cobalamin Malabsorption (FBCM) is seen in 20-40% of those >60 years of age. FBCM is caused by either lack of gastric acid or *H. Pylori* infection. Occasionally it can be seen in younger people especially those with long-term use of drugs (such as histamine (H2) blockers, proton pump inhibitors, or metformin) or gastric resection.

Monitoring and Laboratory Tests

To address potential concerns that high doses of folate may mask manifestations of vitamin B12 deficiency, signs or symptoms of vitamin B12 deficiency should be considered before initiating folic acid supplementation if doses are greater than 1.0 mg. Vitamin B12 levels may be monitored before and during Sandoz Folic Acid therapy if in the opinion of the healthcare professional it is warranted.

Monitor folate level when drugs known to interact with folic acid are taken concomitantly (See 9.4 Drug-Drug Interactions).

Neurologic

Folate supplementation can mask the early symptoms of vitamin B_{12} deficiency (e.g., chronic malaise, sore tongue, numbness of the fingers), potentially allowing more irreversible symptoms of nerve damage to develop. For this reason, when taking more than 400 mcg daily, it is important to check the level of B_{12}. Signs and symptoms of vitamin B_{12} deficiency (e.g., chronic malaise, sore tongue, numbness of the fingers) should be investigated before starting supplementation with folic acid.

7.1 Special Populations

7.1.1 Pregnant Women

There are no known hazards to the use of folic acid in pregnancy, supplements of folic acid are often beneficial.

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. See 10.3 Pharmacokinetics, Special populations and conditions, Pregnancy and Breast-feeding.

7.1.2 Breast-feeding

Folic acid is actively excreted in human 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.

7.1.3 Pediatrics

Pediatrics (<18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of Sandoz Folic Acid in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use. See 4.2 Recommended Dose and Dosage Adjustment.

7.1.4 Geriatrics

Geriatrics: Red cell folate levels and serum folate levels as well as the existence of a cobalamin deficiency, especially in elderly patients should be determined upfront initiating the treatment.

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Folic acid is relatively non-toxic but has rarely caused allergic reactions including erythema, pruritus, and/or urticaria. High doses (e.g. 15 mg/day) have rarely been associated with various gastrointestinal symptoms such as anorexia, nausea, abdominal distention, flatulence and bitter taste and CNS effects such as altered sleep patterns, difficulty concentrating, irritability, overactivity, excitement, mental depression, confusion, and impaired judgment.

8.5 Post-Market Adverse Reactions

Information is not available.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Pregnant and lactating women and people undergoing haemodialysis for kidney disease develop this deficiency because they have an increased need for folic acid.

Pregnant women are more prone to develop folate deficiency that can lead to complications and foetal abnormalities. See 10.3 Pharmacokinetics, Special populations and conditions, Pregnancy and Breast-feeding.

Lactation: Folic acid is actively excreted in human breast milk. Problems in humans have not been documented with intake of normal daily requirements of folic acid during lactation.

9.3 Drug-Behavioural Interactions

Alcohol interferes with the absorption and metabolism of folic acid. Those who drink large amounts of alcohol develop this deficiency.

9.4 Drug-Drug Interactions

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Table 2 – Established or Potential Drug-Drug Interactions

Common name	Source of Evidence	Effect	Clinical comment
Phenytoin, isoniazid, primidone, barbiturates, sulfasalazine, glutethamide, cycloserine, folic acid antagonists (methotrexate, pyrimethamine, triamterene, diamidine compounds, trimethoprim), anticonvulsants, antacids, cholestyramine, colestipol, H_2 blockers, carbamazepine, phenobarbitol, valproate, sulfasalazine, nitrous oxide, and oral contraceptives	C	↓ Folic acid	Decrease absorption of folic acid
Cholestyramine	C	↓ Folic acid	When cholestyramine and folic acid are administered together, there may be a reduction or delay in folic acid absorption. If concomitant therapy is required, folic acid should be administered at least one hour before or 4 to 6 hours after cholestyramine.
Anticonvulsant drugs	T		Folic acid may interfere with the action of anticonvulsant drugs.

Common name	Source of Evidence	Effect	Clinical comment
Phenytoin	T	↓ Phenytoin	Folic acid therapy in folate-deficient individuals may decrease serum levels of phenytoin.
Pancreatin	C		Separate the dose of pancreatin from the dose of folate by at least two hours in order to avoid absorption problems.
Methotrexate	C	↓ Methotrexate	Methotrexate for rheumatoid arthritis, juvenile rheumatoid arthritis, or psoriasis: evidence suggests that folate supplements may reduce side effects of the drug without decreasing its benefits. Nonetheless, physician supervision is highly recommended. If methotrexate is taken for other conditions, folate might decrease the drug's effectiveness. Although folic acid is not effective in the treatment of methotrexate overdose, it is used during long-term methotrexate therapy to prevent or treat associated folate deficiency, prevent methotrexate toxicity and to prevent hyperhomocysteinemia.

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

9.5 Drug-Food Interactions

Interactions with food have not been established.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Folic acid is a water soluble B complex vitamin and is essential in the body for the formation of new cells. It is involved in the metabolism of DNA and RNA, deoxyribonucleic acid and ribonucleic acid respectively, and is required for normal growth, development and functioning of the foetus, nervous system and bone marrow.

Folates act as coenzymes for two sets of cellular reactions. The first involves methylation reactions that are central to amino acid metabolism. For example, folate plays an important role in the conversion of homocystine to methionine. (Vitamin B_{12} is also a coenzyme for this reaction) Methionine is in turn a central building block for proteins. It plays a further role in phospholipids synthesis and creatine-phosphate synthesis, two reactions vital to the survival of the cell and the organism. Folate's second important function as a coenzyme is in the synthesis of nucleic acids, i.e., of DNA and RNA. In this capacity, folate is essential to normal cell replication and embryonic development.

10.2 Pharmacodynamics

Folic acid deficiency can lead to megaloblastic and macrocytic anemias, as a result of impairment of thymidylate synthesis.

Folic acid occurs in a variety of foods in the form of polyglutamate complexes. Folic acid found in pharmaceutical preparations is synthetically derived.

Many plant and animal tissues contain folic acid (pteroylglutamic acid, folacin, vitamin B_2) as reduced methyl or formyl polyglutamates. In the tetrahydro form, folates act as coenzymes for processes in which there is a transfer of a one-carbon unit (e.g., in purine and pyrimidine nucleotide biosynthesis), amino acid conversions (e.g., histidine to glutamic acid through formiminoglutamic acid), generation and use of formate, maturation of RBCs, neural function, DNA synthesis related to folate coenzyme, and methionine synthesis.

Absorption occurs in the gastrointestinal tract (duodenum and upper jejunum). Folic acid is converted in the liver into tetrahydrofolic acid that is a cofactor in the biosynthesis of purines and thymidylates of nucleic acids. An exogenous source of folic acid necessary for the synthesis of nucleoproteins and maintenance of normal erythropoiesis. In the epithelial cells, food polyglutamates are reduced to dihydrofolates and tetrahydrofolates. They are bound to protein and transported as methyltetrahydrofolate. Serum levels vary from 4 to 21 ng/mL (9 to 48 nmol/L) and closely reflect dietary intake. RBC folate (normal, 225 to 640 ng/mL whole blood [510 to 1450 nmol/L] corrected to packed cell volume of 45%) is a better indicator of folate tissue status. Total body folate is about 70 mg, of which 1/3 is found in the liver. About 20% of ingested folate is secreted unabsorbed together with 60 to 90 mcg/day not reabsorbed from bile.

Alcohol interferes with its intermediate metabolism, intestinal absorption, and enterohepatic salvage. Hence marginal dieters and chronic alcoholics are prone to macrocytic anaemia from folate deficiency, as are those with chronic liver disease. Because the foetus obtains folate from

maternal supplies, pregnant women are susceptible to megaloblastic anaemia. In tropical sprue, malabsorption is secondary to the atrophy of intestinal mucosa resulting from the lack of folate, so even minute doses usually correct both anaemia and steatorrhea. Folate deficiency may develop in patients taking long-term anticonvulsant therapy or oral contraceptives, due to decreased absorption, or in patients taking antimetabolites (methotrexate) and antimicrobial drugs (e.g., trimethoprim-sulfa-methoxazole) that interfere with folate metabolism. Increased demand for folate occurs in pregnant and lactating patients with chronic (especially congenital) haemolytic anaemias or psoriasis and in patients on long-term dialysis.

CAUSES OF FOLATE DEFICIENCY

CAUSE	**SOURCE**
Inadequate intake	Diet lacking fresh, slightly cooked food; chronic alcoholism; TPN
Inadequate absorption	Malabsorption syndromes (especially celiac disease, sprue), drugs (phenytoin, primidone, barbiturates, cycloserine, oral contraceptives), folic acid malabsorption (congenital, acquired), blind loop syndrome.
Inadequate utilization	Folic acid antagonists (methotrexate, pyrimethadine, triamterene, diamidine compounds, trimethoprim), anticonvulsants, enzyme deficiency (congenital, acquired), vitamin B_{12} deficiency, alcoholism, scurvy
Increased requirement	Pregnancy, lactation, infancy, malignancy (especially lymphoproliferative), increased haemopoiesis (especially β-thalassemia major), increased metabolism
Increased excretion	Renal dialysis (peritoneal or haemodialysis); vitamin B_{12} dependency, liver disease

Deficiency of folic acid is quite common and can be caused by inadequate intake, problems with absorption and metabolism or increased requirements. Symptoms of severe deficiency include:

- Loss of appetite
- Abdominal pain
- Sickness
- Diarrhoea
- Ulcers in the mouth
- In pregnancy: premature birth and/or malformation
- In children: growth retardation

Folic acid is a B complex vitamin, which after conversion to tetrahydrofolic acid, is necessary for normal erythropoiesis and nucleoprotein synthesis. It is important for carbohydrate metabolism and healthy mucous membranes.

Because Folic Acid is a water-soluble vitamin, it is not stored in the body in appreciable amounts and as a result a daily supply is essential to prevent depletion. Folic acid dependency

results from a genetic defect in the metabolism of the vitamin or in the binding of the vitamin-related coenzyme to its apoenzyme. In some instances, doses much higher than the recommended dietary allowance (RDA) improve the function of the altered metabolic pathway. Patients on long-term dialysis commonly receive multivitamin supplements (to replace estimated dialytic loss of the water-soluble vitamins B-complex, folic acid and vitamin C.

Folic acid and vitamin B_{12} function interdependently in the formation of normal red blood cells and in the production of DNA, and thymidine. A deficiency of either of these vitamins results in a serious anaemia (such as pernicious anaemia), in which the red blood cells are few in number but large in size. Symptoms include paleness, weakness, reduced acid secretion in the stomach, and nerve damage (neuropathy). Nerve damage occurs mainly in vitamin B_{12} deficiency. Folic acid deficiency can lead to megaloblastic and macrocytic anaemias as a result of impairment of thymidylate synthesis. Within 48 hours of beginning treatment with folic acid, the bone marrow of patients with megaloblastic anaemia due to folate deficiency begins to become normoblastic. In megaloblastic anaemias due to folate deficiency, the megaloblastic erythropoiesis disappears within 48 hours of initiation of treatment and the reticulocyte count begins to increase within 2 to 5 days, reaching a maximum at 5 to 7 days.

Folic acid polyglutamates from food sources are enzymatically hydrolized in the gastrointestinal tract to monoglutamates prior to absorption, which occurs mainly in the proximal small intestine. In the presence of malabsorption syndrome, folic acid from oral supplements will still be absorbed whereas absorption of folic acid from food sources may be impaired.

10.3 Pharmacokinetics

Absorption and Distribution:

Following absorption of 1 mg or less, folic acid is converted in the liver and plasma into its metabolically active form tetrahydrofolic acid, which is then distributed into all body tissues.

Metabolism:

The liver contains about 50% of total body folate stores. Larger doses of folic acid may escape metabolism by liver and appear in the blood mainly as folic acid.

Elimination:

Following oral administration of single 0.1 to 0.2 mg doses of folic acid in healthy adults, only a trace amount of the drug appears in urine. Following administration of large doses, the renal tubular reabsorption maximum is exceeded, and excess folate is excreted unchanged in urine. After doses of about 2.5 to 5.0 mg, about 50% of a dose is excreted in urine and after a 15 mg dose, up to 90% may be recovered in urine. Small amounts of orally administered folic acid have been recovered from feces.

Special Populations and Conditions

- **Pediatrics:** The clinical trial data on which the indication was originally authorized is not available.

- **Geriatrics:** The clinical trial data on which the indication was originally authorized is not available.
- **Sex:** The clinical trial data on which the indication was originally authorized is not available.
- **Pregnancy and Breast-feeding:** Studies have provided strong scientific support for periconceptual prophylaxis with folic acid in reducing the risk of foetal neural tube defects. Folic acid deficiency may occur in pregnant women on diets that lack green leafy vegetables and legumes that contain folic acid. Infants may develop folic acid deficiency when the folic acid content of their formula is low. Treatment of folic acid deficiency consists of folic acid taken orally. Infants may have neurological abnormalities, and this deficiency in a pregnant woman can cause spinal cord defects and other malformations of the foetus.
- **Genetic Polymorphism:** The clinical trial data on which the indication was originally authorized is not available.
- **Ethnic Origin:** The clinical trial data on which the indication was originally authorized is not available.
- **Hepatic Insufficiency:** The clinical trial data on which the indication was originally authorized is not available.
- **Renal Insufficiency:** The clinical trial data on which the indication was originally authorized is not available.
- **Obesity:** The clinical trial data on which the indication was originally authorized is not available.

11 STORAGE, STABILITY AND DISPOSAL

Store at room temperature between 15°C and 30°C.

Keep out of reach of children. This product contains sufficient drug to seriously harm a child.

Sandoz Folic Acid should never be disposed of in household trash. Disposal via a pharmacy take back program is recommended.

12 SPECIAL HANDLING INSTRUCTIONS

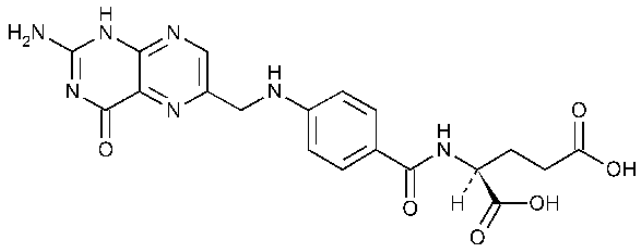
No special handling required.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name:	folic acid
Chemical name:	Information is not available
Molecular formula and molecular mass:	$C_{19}H_{19}N_7O_6$ 441.40 g / mol
Structural formula:	



Physicochemical properties:	Information is not available
Pharmaceutical standard:	USP

14 CLINICAL TRIALS

The clinical trial data on which the original indication was authorized is not available.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology: Information is not available.

Carcinogenicity: Information is not available.

Genotoxicity: Information is not available.

Reproductive and Developmental Toxicology: Information is not available.

Special Toxicology: Information is not available.

Juvenile Toxicity: Information is not available.

17 SUPPORTING PRODUCT MONOGRAPHS

1. Pr FOLIC ACID, Folic Acid Tablets, 5mg, Product Monograph, Submission Control: 258037, AA Pharma. APR 7, 2022.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr] Sandoz® Folic Acid

Folic Acid tablets USP

Read this carefully before you start taking **Sandoz Folic Acid** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Sandoz Folic Acid**.

What is Sandoz Folic Acid used for?

Sandoz Folic Acid is a prescription medicine used:

- to prevent and treat folate deficiency. This is means that you have low levels of folic acid in your blood. This will be confirmed by a healthcare professional. Your folate deficiency may be because:
    - you have a poor diet,
    - your body does not use or absorb folate well from your food,
    - you are on kidney dialysis,
    - you have hemotyic anemia. This is a condition where red blood cells are destroyed faster than the body can make them.
    - you are a pregnant woman, an infant or a child with megoblastic anemia. This is a condition where you have large, abnormal red blood cells,
    - you have liver problems,
    - you suffer from alcoholism and have cirrhosis of the liver (liver failure), or
    - you are taking medicines to treat seizures called anticonvulsants.
- to prevent birth defects in the babies of women who:
    - are planning to get pregnant or are pregnant,
    - have previously had a pregnancy where the baby had a neural tube defect,
    - have diabetes or conditions where their bodies do not absorb folic acid or
    - are taking anticonvulsant medicines or other medicines that affect how folic acid is used by cells of the body.
- to prevent side effects related to treatment with low doses of methotrexate. These side effects may include:
    - sores in your mouth and irritation of the gastrointestinal tract, and
    - low levels of folate and high levels of homocysteine in the blood

Even if you are taking Sandoz Folic Acid, you should still eat a balanced diet.

How does Sandoz Folic Acid work?

Sandoz Folic Acid is a vitamin. It is essential for the body to make new cells. It helps the body make DNA and RNA. Sandoz Folic Acid is needed for normal growth, development and function of the foetus, nervous system and bone marrow.

What are the ingredients in Sandoz Folic Acid?

Medicinal ingredients: folic acid

Non-medicinal ingredients: colloidal silicon dioxide, croscarmellose sodium, magnesium stearate, magnesium trisilicate, microcrystalline cellulose, pregelatinized starch.

Sandoz Folic Acid comes in the following dosage forms:

Tablets: 5 mg

Do not use Sandoz Folic Acid if:

- you are allergic to folic acid, to products that contain Sandoz Folic Acid or to any of the other ingredients of this medicine.
- you have problems with your small intestine, especially Crohn's disease (type of inflammatory bowel disease) and sprue (malabsorption disease).
- you have a vitamin B_{12} deficiency and are not receiving treatment for it. A vitamin B_{12} deficiency means that you have very low levels of vitamin B_{12} (cobalamin) in your blood.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Sandoz Folic Acid. Talk about any health conditions or problems you may have, including if you:

- are taking large doses of vitamins. This is called megavitamin therapy.
- suffer with pernicious anemia. This is a condition where the body does not make enough red blood cells due to low levels of vitamin B_{12}. If you have this condition, your healthcare professional may recommend that you take vitamin B_{12}.
- have Food-Bound Cobalamin Deficiency. This is a condition where your body can't obtain vitamin B_{12} (cobalamin) from the food you eat.
- are undergoing dialysis for kidney disease.
- are taking any herbal supplements.
- are taking cholestyramine.
- have lactose intolerance. This is because this medicine contains lactose.

Other warnings you should know about:

Taking high doses (or large amounts) of Sandoz Folic Acid, may:

- hide a vitamin B_{12} deficiency. A vitamin B_{12} deficiency can cause anemia (low levels of red blood cells) and nerve damage. Taking large amounts of folate can fix the anemia, but not the nerve damage. This means the nerve damage may be permanent and could affect your brain, spinal cord, or other nerves.
- make the symptoms of vitamin B_{12} deficiency worse.

- increase your risk for cancer of the colon or rectum. It may also increase the risk for other cancers in some people.

Pregnancy:

- Taking Sandoz Folic Acid during pregnancy is helpful. It can help prevent birth defects and neural tube defects in the baby.
- Low levels of folic acid in the blood during pregnancy can cause miscarriage. It may also affect how the baby grows in the womb.
- Taking some other medicines during pregnancy can cause birth defects or neural tube defects in the baby. This is because these medicines can:
    - affect how folic acid is broken down in the body, or
    - cause low levels of folic acid in the blood.

Blood tests:

Before you start taking Sandoz Folic Acid, your healthcare professional will do blood tests. These tests will measure the amount of folate and vitamin B12 in your blood as well as the level red blood cells. These tests may be repeated during your treatment, especially if you are taking medicines that can interact with Sandoz Folic Acid.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with Sandoz Folic Acid:

- medicines used to treat epilepsy and seizures such as phenytoin, primidone, carbamazepine, phenobarbital, valproate / valproic acid.
- medicines used to treat depression called barbiturates.
- medicines used to treat tuberculosis including isoniazid and cycloserine.
- a medicine used to treat ulcerative colitis, Crohn's disease or rheumatoid arthritis called sulfasalazine.
- a medicine used to treat insomnia called glutethamide.
- medicines called folic acid antagonists. These include:
    - Methotrexate, which is used to treat Crohn's disease, rheumatoid arthritis or cancer;
    - Pyrimethamine, which is used to treat malaria;
    - Triamterene. This is a diuretic (water pill), which is used to treat high blood pressure or swelling;
    - Trimethoprim, diamidine compounds, which are used to treat infections.
- medicines used to treat indigestion called antacids.
- medicines used to lower cholesterol including cholestyramine and colestipol.
- medicines used to treat ulcers called H2 blockers.
- a medicine used as an anesthetic and to treat pain called nitrous oxide.
- birth control medicines that are taken by mouth.
- a medicine used to treat digestion problems called pancreatin.

Alcohol can lower Sandoz Folic Acid levels in the body. Do not consume alcohol if you have low folic acid levels in your body.

How to take Sandoz Folic Acid:

Take Sandoz Folic Acid:

- exactly as directed by your healthcare professional. Ask your doctor, nurse or pharmacist if you are not sure.
- Take Sandoz Folic Acid tablets by mouth, once per day.
- Do not use if seal is broken.

Usual dose: Your healthcare professional will tell you how much Sandoz Folic Acid to take. This will depend on:

- the condition that you are being treated for,
- your age, and
- whether you are taking other medicines or vitamins.

Overdose:

The symptoms of overdose may include bitter taste, loss of appetite, nausea, gas, nightmares, agitation, and depression. If you are taking medicines to treat epilepsy or seizures (such as phenobarbital, phenytoin or primidone), you may have seizures more often. They may also be stronger.

If you think you, or a person you are caring for, have taken too much Sandoz Folic Acid, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you forget to take a dose, take it as soon as you remember. If it is nearly time for the next dose, skip the missed dose and take the next dose at the right time. Do NOT take more than one dose at time to make up for a forgotten dose.

What are possible side effects from using Sandoz Folic Acid?

These are not all the possible side effects you may have when taking Sandoz Folic Acid. If you experience any side effects not listed here, tell your healthcare professional.

- loss of appetite
- nausea
- abdominal bloating
- gas
- bitter taste
- change in sleep
- trouble concentrating
- feeling irritable, excited, overactive, confused

- impaired judgment

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
RARE			
Allergic reactions: skin redness, itching, skin rash or sudden outbreak of pale red bumps or welts on the skin (hives)	√		
Depression (a sad mood that won't go away): difficulty sleeping or sleeping too much, changes in appetite or weight, withdrawal from social situations, reduced sex drive, thoughts of death or suicide.		√	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at room temperature between 15°C and 30°C.

Keep out of reach and sight of children. This product contains sufficient drug to seriously harm a child.

If you want more information about Sandoz Folic Acid:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html). Find the Product Monograph on the manufacturer's website (www.sandoz.ca), or by calling 1-800-361-3062.

This leaflet was prepared by Sandoz Canada Inc.

Last Revised: November 18, 2022