SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Folic acid Colonis 1 mg/ml oral solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of oral solution contains 1 mg of folic acid.

Excipients with known effect:
Sodium methyl parahydroxybenzoate (E219)
Sodium

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution

Clear, yellow and odourless solution

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

1. For the prophylaxis of neural tube defects in case of a positive history of previous neural tube defects (NTD).

2. For the prophylaxis of NTDs with no previous history of foetal neural tube defect and no other predisposing factors

3. For the treatment of folate deficiency:
    a. Folate deficient megaloblastic anaemia (in pregnancy, associated with alcoholism, drug intake such as anticonvulsants). For the prevention of megaloblastic anaemia, the cobalamin status should be established before initiation of folic acid therapy.

b. Impaired utilization of folate i.e. use of concomitant drugs, in liver disease, inadequate intake (e.g. alcoholism, malnutrition etc.)

c. Increased excretion of folate (e.g. alcoholism, haemolytic states).

4. Folate deficiency / megaloblastic anaemia associated with haemolytic anaemia (e.g. sickle cell anaemia)

5. Treatment of folate deficiency in malabsorption syndromes (parenteral administration of folic acid may need to be considered if oral treatment is not effective)

(e.g.: tropical sprue. tropical sprue responds to folate supplements in the early stages of the disease but cobalamin status must also be checked, particularly later; coeliac disease in which case the necessity of supplementation with folate ceases once a gluten free diet is introduced; non-tropical sprue; in congenital folate malabsorption (oral treatment may not be effective and parental folate may therefore be required).

Cobalamin status needs to be established in all megaloblastic states (not only in pregnancy).

4.2 Posology and method of administration

For oral administration only.

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: 5 mg every 1-7 days depending on underlying disease.

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

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

- In pregnancy with no previous history of foetal NTD and no other predisposing factors: 0.4 mg daily until 10 to 12 weeks after last menstrual period

Paediatric population:

- 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.

The duration of the folic acid regimen has not been determined precisely in all patient populations, but it is recommended to administer the vitamin until the formation of new colonies of red blood cells is observed.

Depending on the etiological factor, diet improvement, removal of etiological factor, treatment of an inflammation may lead to cessation of treatment. In cases of haemolytic anaemia or in cases of concomitant drug intake, a longer treatment may be necessary in order to prevent occurrence of haematological disorders.

Method of administration

A graduated oral syringe and a Press-In Bottle Adapter (PIBA) are provided with the product.

1. Open the bottle and at first use insert the Press-In Bottle Adapter (PIBA).
2. Insert the syringe into the PIBA and draw out the required volume from the inverted bottle.
3. Remove the filled syringe from the bottle in the upright position
4. Discharge the syringe contents into the mouth. Repeat steps 2 to 4 as needed to achieve the required dose.
5. Rinse the syringe and replace the cap on the bottle (PIBA remains in place).

4.3 Contraindications

Known hypersensitivity to folic acid.

Known hypersensitivity to hydroxybenzoate esters.

Folic acid should not be given alone in the treatment of Addisonian pernicious anaemia and other vitamin B_{12} deficiency states because it may precipitate the onset of subacute combined degeneration of the spinal cord. In elderly people, a cobalamin absorption test should be done before long-term folate therapy.

Folic acid given to patients for 3 months or longer has precipitated cobalamin neuropathy. No harm results from short courses of folic acid.

Folic acid should not be used in folate-dependent tumours or malignant disease unless megaloblastic anaemia owing to folate deficiency is an important complication.

4.4 Special warnings and precautions for use

If folic acid is used indiscriminately, there is a danger that patients with pernicious anaemia and other B_{12} deficiency states, despite a haematological remission, may develop irreparable neurological lesions. Therefore a full clinical diagnosis should be made before initiating treatment.

Folic acid is removed by haemodialysis.

The therapeutic effect should be monitored by laboratory analysis and the diagnosis should be reassessed (specialist workup) in case the expected response fails to appear. Serum Potassium levels and iron/ferritin status should be controlled.

Cobalamin status needs to be established in all megaloblastic states (not only in pregnancy).

Excipient warnings

Folic acid Colonis 1 mg/ml oral solution contains sodium methyl parahydroxybenzoate (E219) and sodium

- Sodium methyl parahydroxybenzoate (E219) may cause allergic reactions (possibly delayed).
- This medicine contains less than 1 mmol sodium (23 mg) per 1 ml that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Antiepileptics – if folic acid supplements are given to treat folate deficiency, which can be caused by the use of antiepileptics (phenytoin, phenobarbital and primidone), the serum antiepileptic levels may fall, leading to decreased seizure control in some patients.

Antibiotics – chloramphenicol and co-trimoxazole may interfere with folate metabolism.

Sulfasalazine - can reduce the absorption of folic acid.

Folic acid may interfere with the toxic and therapeutic effects of methotrexate.

4.6 Fertility, pregnancy and lactation

Pregnancy

The product is indicated for use during pregnancy.

There are no known hazards from the use of folic acid in pregnancy; indeed folic acid supplements are often beneficial in pregnancy. There is published evidence that folic acid is beneficial in the prevention of neural tube defects. Lack of the vitamin or its metabolites may also be responsible for some cases of spontaneous abortion and intrauterine growth retardation.

Lactation

Folic acid is actively excreted in 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.

Fertility

There are no known risks from the use of folic acid on fertility. See sub section "Pregnancy".

4.7 Effects on ability to drive and use machines

There are no known effects of this preparation on the ability to drive or use machines.

4.8 Undesirable effects

Rare (≥ 1/10,000 to <1/1,000)	Gastrointestinal disorders: Loss of appetite, nausea, abdominal distension and flatulence.
	Immune system disorders: Allergic reactions such as erythema, rash, itching, urticaria, difficulty in breathing and anaphylactic reactions (including shock)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard

4.9 Overdose

No cases of acute overdosage appear to have been reported, but even extremely high doses are unlikely to cause harm to patients.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: B03BB01

After conversion into co-enzyme forms it is concerned in single carbon unit transfers in the synthesis of purines, pyrimidines and methionine.

5.2 Pharmacokinetic properties

About 70-80% of a 2 mg oral solution of folic acid is absorbed. Larger doses are probably equally well absorbed. It is distributed into plasma and extracellular fluid. In plasma, folate is bound weakly to albumin (70%). There is a further high affinity binder for folate but this has a very low capacity and is barely detectable in normal sera. About 70% of small doses of folate (about 1 mg) are retained and the rest excreted into the urine. With larger doses most is excreted into the urine. With a 5 mg dose of folate, urinary excretion will be complete in about 5 hours. There is an enterohepatic circulation of folate. The retained folate is taken into cells and reduced by dihydrofolate to tetrahydrofolate. Folic acid is a relatively poor substrate for folate reduction, the normal substrate being dihydrofolate.

Folic acid itself does not occur in natural materials, it is entirely a pharmacological form of the compound. Once reduced, folate has additional glutamic acid residues added, a folate pentaglutamate being the dominant intracellular analogue. These polyglutamates are the active co-enzymes.

5.3 Preclinical safety data

Effects in non-clinical studies were only observed at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Methyl Parahydroxybenzoate (E219)

Disodium Edetate (E385)

Mannitol (E421)

Hydrochloric Acid, Concentrated (E507)

Water, Purified

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months

After first opening do not store above 25°C and use within 3 months.

6.4 Special precautions for storage

Do not store above 25°C. Keep bottle in the outer carton.

6.5 Nature and contents of container

Folic acid oral solution 1 mg/ml is packed in amber (Type III) glass bottle 150 ml, with child-resistant, tamper-evident screw cap with an LDPE liner, a 5 ml graduated oral dosing syringe and a “press-in” syringe/bottle adaptor (PIBA).

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Colonis Pharma Limited
25 Bedford Square
Bloomsbury
London
WC1B 3HH

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 41344/0024

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

17/10/2016

10 DATE OF REVISION OF THE TEXT

21/03/2024