# Summary of Product Characteristics

## 1. Name of the medicinal product
**FOLIK tablets 5 mg**
*FOLIK*

## 2. Qualitative and quantitative composition
Each FOLIK tablets contains 5 mg FOLIK.
For excipients, see Section 6.1.

## 3. Pharmaceutical form
Tablet.

## 4. Clinical particulars
### 4.1 Therapeutic indications

FOLIK is necessary for the normal production and maturation of blood cells and is used in the treatment of nutritional megaloblastic anaemias e.g., megaloblastic anaemia following gastrectomy and the megaloblastic anaemia of pregnancy.
It may also be used prophylactically in chronic haemolytic states or in renal dialysis.

### 4.2 Posology and method of administration

Adults
For nutritional megaloblastic anaemia a dose of 1 tablet daily for up to 4 months is normally sufficient but up to 15 mg daily may be required where malabsorption exists.
A maintenance dose of 5 mg every 1 to 7 days may also be required.
Children
In children over 1 year the dose is as for adults.
Administration – Oral.

### 4.3 Contraindications

Long-term folate therapy is contraindicated in any patient with untreated cobalamin deficiency. This can be untreated pernicious anaemia or other cause of cobalamin deficiency, including lifelong vegetarians. In elderly people, a cobalamin absorption test should be done before long-term folate therapy. Folate given to such patients for 3 months or longer has precipitated cobalamin neuropathy. No harm results from short courses of folate.
FOLIK should never 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.
FOLIK should not be used in malignant disease unless megaloblastic anaemia owing to folate deficiency is an important complication.
Known hypersensitivity to FOLIK or any of the excipients.

### 4.4 Special warnings and precautions for use

Patients with vitamin $B_{12}$ deficiency should not be treated with FOLIK unless administered with adequate amounts of hydroxocobalamin, as it can mask the condition but the subacute irreversible damage to the nervous system will continue. The deficiency can be due to undiagnosed megaloblastic anaemia including in infancy, pernicious anaemia or macrocytic anaemia of unknown aethiology or other cause of cobalamin deficiency, including lifelong vegetarians.
Caution should be exercised when administering FOLIK to patients who may have folate dependent tumours.

This product is not intended for healthy pregnant women where lower doses are recommended, but for pregnant women with FOLIK deficiency or women at risk for the reoccurrence of neural tube defect.

### 4.5 Interaction with other medicinal products and other forms of interaction

There is a specific interaction between phenytoin and folate such that chronic phenytoin use produces folate deficiency. Correction of the folate deficiency reduces plasma phenytoin with potential loss of seizure control. Similar but less marked relationship exist with all anti-convulsant treatments including sodium valproate, carbamazepine and the barbiturates. Sulphasalazine and triamterene also inhibit absorption.
Antibacterials, chloramphenicol and co-trimoxazole, may interfere with folate metabolism.
Folate supplements enhance the efficacy of lithium therapy. Methotrexate and trimethoprim are specific anti-folates and the folate deficiency caused by their prolonged use cannot be treated by FOLIK Tablets BP. Folinic acid should be used. Nitrous oxide anaesthesia may cause an acute FOLIK deficiency. Both ethanol and aspirin increase folic elimination.

### 4.6 Fertility, pregnancy and lactation

Pregnancy
There are no known hazards to the use of FOLIK in pregnancy, supplements of FOLIK are often beneficial. Non-drug - induced FOLIK deficiency, or abnormal folate metabolism, is related to the occurrence of birth defects and some neural tube defects. Interference with FOLIK 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.
Lactation
FOLIK is actively excreted in human breast milk. Accumulation of folate in milk takes precedence over maternal folate needs. Levels of FOLIK 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 FOLIK.

### 4.7 Effects on ability to drive and use machines

No effect on concentration and co-ordination.

### 4.8 Undesirable effects

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|---|---|
| **Gastrointestinal disorders**<br>Rare (≥1/10,000 til <1/1,000) | Anorexia, nausea, abdominal distension and flatulence |
| **Immune system disorders**<br>Rare (≥1/10,000 til <1/1,000)<br>Not known (frequency cannot be estimated from the available data) | Allergic reactions, comprising erythema, rash, pruritus, urticaria, dyspnoea, and shock.<br>Anaphylactic reaction |

**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.

### 4.9 Overdose

There are no specific symptoms of overdosage and similarly no emergency treatment or antidotes, metabolisation and excretion can be rapid.

## 5. Pharmacological properties

### 5.1 Pharmacodynamic properties

ATC Code: **B03B B01 FOLIK and derivatives.**
FOLIK is a member of the vitamin B group which is reduced in the body to tetrahydrofolate, a co-enzyme active in several metabolic processes and produces a haemopoietic response in nutritional megaloblastic anaemias (but see warning in Section 4.4 regarding need for concomitant use of hydroxycobalamin).
FOLIK is rapidly absorbed and widely distributed in body tissues.

### 5.2 Pharmacokinetic properties

Absorption – FOLIK is rapidly absorbed from the gastrointestinal tract, mainly from the proximal part of the small intestine. Dietary folates are stated to have about half the bioavailability of crystalline FOLIK. The naturally occurring folate polyglutamates are largely deconjugated and reduced by dihydrofolate reductase in the intestine to form 5-methyltetrahydrofolate (5MTHF). FOLIK given therapeutically enters the portal circulation largely unchanged, since it is a poor substrate for reduction by dihydrofolate reductases.
Distribution – via portal circulation. 5MTHF from naturally occurring folate is extensively plasma bound. The principal storage site of folate is in the liver; it is also actively concentrated in the CSF. Folate is distributed into breast milk.
Metabolism – therapeutically given FOLIK is converted into the metabolically active form 5MTHF in the plasma and liver. There is an enterohepatic circulation for folate.
Elimination – Folate metabolites are eliminated in the urine and folate in excess of body requirements is excreted unchanged in the urine. FOLIK is removed by haemodialysis.

### 5.3 Preclinical safety data

There is no pre-clinical data of relevance to a prescriber which is additional to that already included in other sections of the SPC.

## 6. Pharmaceutical particulars

### 6.1 List of excipients

- microcrystalline cellulose
- croscarmellose sodium
- colloidal silicon dioxide
- sodium lauryl sulfate
- magnesium stearate.

### 6.2 Incompatibilities

None known.

### 6.3 Shelf life

2 years.

### 6.4 Special precautions for storage

Do not store above 25°C.

### 6.5 Nature and contents of container

Box of 20 round tablets, yellow of 5 mg folic acid in blister pack (2 blisters x 10 tablets).

## 6.6 Special precautions for disposal and other handling

FOLIK Tablets 5 mg are for oral administration only.
Keep all medicines out of the reach of children.
Do not use after the expiry date.

## 7. Marketing authorisation holder

ZADA Pharmaceuticals Ltd.
Donji Bistarac  without number
75 300 Lukavac
Bosnia and Herzegovina

## 8. Marketing authorisation number(s)

FOLIK, 20 tablets of 5 mg in box: 04-07.3-2-5150/15

## 9. Date of renewal of the marketing authorisation

FOLIK, 20 tablets of 5 mg in box: 20.11.2015.

## 10. Date of revision of the text

8th May 2018