PRESCRIBING INFORMATION

1. NAME OF THE MEDICINAL PRODUCT
Folic Acid 5 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Folic Acid 5mg

Excipients with known effect
Lactose

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM
Tablets
Round, biconvex tablets, contains orange to red granules, “R” engraved on one side.
The tablet can be halved or crushed to make it easier to swallow.

4. CLINICAL PARTICULARS
4.1. Therapeutic Indications
For the treatment of megaloblastic anemias caused by folic acid deficiency.

4.2 Posology and method of administration
Posology
One tablet a day.
Method of administration
The tablets are for oral use.

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Patients with malignant disease, unless megaloblastic anaemia due to folic acid deficiency.

4.4 Special warnings and precautions for use
Folic acid should not be administered for treatment of pernicious anaemia or undiagnosed megaloblastic anaemia without sufficient amounts of cyanocobalamin (vitamin B12) as folic acid alone will not prevent and may precipitate development of subacute combined degeneration of the spinal cord. Therefore a full clinical diagnosis should be made before initiating treatment.

Folate should not be routinely used in patients receiving coronary stents.

Caution should be exercised when administering folic acid to patients who may have folate dependent tumours.

Folic acid is removed by haemodialysis.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
Absorption of folic acid may be reduced by sulfasalazine.

Concurrent administration with cholestyramine may interfere with folic acid absorption. Patients on prolonged cholestyramine therapy should take folic acid 1 hour before or 4 to 6 hours after receiving cholestyramine.
Antibiotics may interfere with the microbiological assay for serum and erythrocyte folic acid concentrations and may cause falsely low results.

Trimethoprim or sulphonamides, alone or in combination as co-trimoxazole, may reduce the effect of folic acid and this may be serious in patients with megaloblastic anaemia.

Serum levels of anticonvulsant drugs (phenytoin, phenobarbital, primidone) may be reduced by administration of folate and therefore patients should be carefully monitored by the physician and the anticonvulsant drug dose adjusted as necessary.

Fluorouracil toxicity may occur in patients taking folic acid and this combination should be avoided.

Edible clay or antacids containing aluminium or magnesium may reduce folic acid absorption. Patients should be advised to take antacids at least two hours after administration of folic acid.

Folic acid may reduce intestinal absorption of zinc (of particular importance in pregnancy).

4.6 Fertility, pregnancy and lactation

Pregnancy
Folic acid deficiency during pregnancy may lead to the appearance of foetal malformations. Imbalance in folate requiring trophoblast cells may also lead to detachment of the placenta.

Very high doses of folic acid have been shown to cause foetal abnormalities in rats; however, harmful effects in the human foetus, mother or the pregnancy have not been reported following ingestion of folic acid.

Breastfeeding
Folic acid is excreted in breast milk.
No adverse effects have been observed in breast-fed infants whose mothers were receiving folic acid.

4.7. Effects on Ability to Drive and Use Machines
None known.

4.8 Undesirable effects
Folic acid is generally well tolerated although the following side effects have been reported:

Blood and lymphatic system disorders:
Folic acid may worsen the symptoms of co-existing vitamin B_{12} deficiency and should never be used to treat anaemia without a full investigation of the cause.

Immune system disorders:
Rare: Allergic reactions, comprising erythema, rash, pruritus, urticarial, dyspnoea, and anaphylactic reactions (including shock).

Gastrointestinal disorder:
Abdominal distension, flatulence, anorexia and nausea.

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form
https://sideeffects.health.gov.il

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. No special procedures or antidote are likely to be needed.

5. Pharmacological Properties

5.1. Pharmacodynamic Properties
The mucosa of the duodenum and upper part of the jejunum are rich in dihydrofolate reductase, where folates and folic acid are absorbed. Once absorbed, folic acid is rapidly reduced and then methylated to form tetrahydrofolic acid derivatives which are rapidly transported to the tissues.

5.2. Pharmacokinetic Properties
Folic acid is readily absorbed following oral dosage, and is extensively bound to plasma proteins.

5.3. Preclinical Safety Data
Toxicity studies in animals (rats and rabbits) have shown that massive doses (100mg/kg upwards) produce precipitation of folate crystals in renal tubules, particularly proximal tubules and ascending limb of the loop of Henle.
Tubular necrosis is followed by recovery.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients
Lactose 100 mesh
Microcrystalline Cellulose (Avicel PH 101)
Maize starch
Ac-di-sol Aerosil 200
Magnesium stearate

6.2. Incompatibilities

None known.

6.3 Shelf life
The expiry date of the product is indicated on the packaging materials.

6.4. Special Precautions for Storage
Store in a dry place below 25°C.

6.5. Nature and Contents of Container
PVC-Aluminium blisters containing 30 tablets and 250 tablets.
Not all package sizes may be marketed.

6.6 Special precautions for disposal
No special requirements.

7. MARKETING AUTHORISATION HOLDER
Rekah Pharmaceutical Industry Ltd., 30 Hamelacha St., Holon, Israel.

8. MARKETING AUTHORISATION NUMBER
128-85-21928-00

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