1. NAME OF THE MEDICINAL PRODUCT

Alben Folic acid Tablet 5mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:
Folic acid Tablet BP……..5mg

Excipients with known effect:

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

- Tablet
- A Yelow circular tablet.

4. Clinical Particulars

4.1 Therapeutic indications

- Treatment of folate deficiency states (e.g. folate deficient megaloblastic anaemia) confirmed by blood test including B12 status (see section 4.4) for adults, children (from 6 years on) and adolescents.
- Prophylaxis of drug-induced folate deficiency (see section 4.5)
- Prevention of neural tube defects in the foetus for women planning a pregnancy and known to be at risk.

4.2 Posology and method of administration

Dosage
Adults
In folate deficient megaloblasticanaemia:
5mg daily for 4 months
Up to 15mg daily may be necessary for malabsorption states
For prophylaxis in chronic haemolytic states or in renal dialysis:
5mg every 1-7 days depending on diet and underlying disease.
In drug induced folate deficiency:
5mg daily
Prevention of recurrence of neural tube defects
5mg daily starting before conception and continuing throughout the first trimester of pregnancy is recommended.
Children
Over 1 year: As adult dose
Up to 1 year: 500µg/kg daily
Method of Administration: For oral administration only.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients. Patients with malignant disease, unless megaloblasticanaemia due to folic acid deficiency.

4.4 Special warnings and precaution for use

Patients with vitamin B12 deficiency should not be treated with folic acid unless administered with adequate amounts of hydroxocobalamin, as it can mask the condition, or the development of such, at risk of serious neurological damage. This can be detected by analysis of methylmalonic acid in plasma.
Since folate may stimulate cell partition, caution should be shown when treating patients with folate dependent tumour disease. Folic acid supplements may increase growth of already existing malignity.
This product is not intended for healthy pregnant women where lower doses are recommended, but for pregnant women with folic acid deficiency or women at risk for the reoccurrence of neural tube defects.

4.5 Interactions with other medicinal products and other forms of interaction

Drugs influenced by concomitant administration of folic acid
Serum levels of anticonvulsant drugs (phenytoin, phenobarbital, primidone and possibly carbamazepine) 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.
Antibacterial agents in the therapeutic subgroup sulphonamides and sulfasalazine.
Fluorouracil and fluorouracil prodrugs toxicity may occur in patients taking folic acid and therefore this combination should be avoided.
Folic acid possibly enhances the toxicity of capecitabine.
Drugs influencing levels of folic acid
Folate deficiency states may be produced by oral contraceptives, anticonvulsants, antituberculosis drugs, alcohol, glucarpidase, and folic acid antagonists such as methotrexate, pyrimethamine, triamterene, trimethoprim, and sulfonamides.
Absorption of folic acid may be reduced by sulfasalazine.

4.6 Pregnancy and Lactation

Pregnancy
Based on the human experience 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.
Breast-feeding
Folic acid is actively excreted into breast milk (see section 5.2). 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; therefore it is usually compatible with breast-feeding.

4.7 Effects on ability to drive and use machines

Folic acid has no influence on the ability to drive and use machines.

4.8 Undesirable effects
Very rare: Hypersensitivity, Anorexia, nausea, vomiting, diarrhoea, flatulence, Rash, pruritus, erythema, urticaria, facial angioedema.

4.9 Overdose

Overdose generally produces no symptoms and symptomatic treatment of overdose should only be required in exceptional cases.

5. Pharmacological properties:

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Folic acid and derivatives, ATC code: B03BB01
Folic acid is a component of coenzymes involved in certain transmethylation processes, such as deoxyribonucleic acid and ribonucleic acid synthesis. Folic acid is one of the B vitamins and is necessary for the normal production and maturation of red blood cells. Folic acid deficiency is one of the causes megaloblastic anaemia.

5.2 Pharmacokinetic properties

Absorption
Folic acid 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 folic acid. The naturally occurring folate polyglutamates are largely deconjugated and reduced by dihydrofolate reductase in the intestine to from 5-methyltetrahydrofolate (5MTHF). Folic acid given therapeutically enters the portal circulation largely unchanged, since it is a poor substrate for reduction by dihydrofolate reductases. Bioavailability of the folic acid is around 85%when administered with food and around 100% when taken on empty stomach.
Distribution
Absorbed folic acid is transported to the liver, which contains about half the body pool of folate and retains 10 to 20% of absorbed folate due to the first-pass effect, while the rest is transported via the systemic circulation to body tissues.
Folic acid crosses the blood brain barrier. Folic acid is excreted into breast milk.
Folic acid crosses the placenta. The mechanism of folate transport across the placenta is established within the first trimester of pregnancy to satisfy the high requirements for folate during foetal development (see section 4.6). As a result of the high folate concentration in the intervillous blood, folate in foetal blood is two to four times higher than in maternal blood.
Biotransformation
Folate, dihydrofolate and tetrahydrofolate are actively reduced and methylated to methyltetrafolate in the liver, which is then transported to the bile and secreted in order then to be reabsorbed via the intestines (enterohepatic cycle). Folates which are not bound to specific and non-specific binding proteins are subjected to catabolism by oxidative cleavage, generating p-aminobenzoylglutamates which in turn are acetylated in the liver before excretion.
Elimination
Folic acid metabolites are eliminated in the urine and folate in excess of body requirements is excreted unchanged in the urine.
Folic acid is removed by haemodialysis.
Folate is secreted via breast milk. Folic acid supplementation in well-nourished lactating women does not affect breast milk folate concentration, whereas, in women with severe folate deficiency, supplementation increases the folate concentration of breast milk even before any improvement in maternal folate status is seen (see section 4.6).

5.3 Preclinical safety data

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, toxicity to reproduction and development.

Mutagenic and carcinogenic potential:
No mutagenic effects are to be expected in physiological doses.
Long-term studies on the carcinogenic potential of folic acid are not available.

6. Pharmaceutical particulars

6.1 List of excipients

- Starch
- Lactose
- Povidone
- Sodium Propyl Paraben
- Crosscarmellose Sodium
- Magnesium stearate

6.2 Incompactibilities

- None relevant known.

6.3 Shelf life

- 36 Months

6.4 Special precautions for storage

- Do not store above 30°C

- Store in a cool dry place protected from light and out of reach of children.

6.5 Nature and contents of container<and special equipment for use, administration or implantation>

- Pack of 1000 tablets contained in a screw cap plastic container.

6.6 Special precautions for disposal<and other handling>

- None.

7. Applicant/Manufacturer

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