SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

FOLAS 5 mg tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance(s):
Each tablet contains folic acid hydrate equivalent to 5 mg folic acid.

Excipient(s):
Lactose monohydrate (derived from cow's milk) 105.5 mg/tablet

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Oral tablet
Yellow, round, flat tablets with a notch on one side, which may contain red spots.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

FOLAS is indicated for the treatment of tropical or nontropical sprue, diet-induced anemias, megaloblastic anemias due to folic acid deficiency in pregnant women, infants or children.

4.2. Posology and method of administration

Posology/frequency of administration and duration of the treatment:
For the treatment of megaloblastic anemia due to folate deficiency, folic acid is used 5 mg (1 tablet) daily for 4 months; in cases of malabsorption, it can be increased up to 15 mg (3 tablets) daily.

In chronic hemolytic conditions such as Mediterranean anemia or sickle cell anemias, prophylactic administration of 5 mg folic acid (1 tablet) daily or weekly may be necessary.

Method of administration:
For oral use.

Additional informations for special populations:
Renal/Hepatic failure:
In kidney patients undergoing dialysis, 5 mg folic acid (1 tablet) per day or week may be necessary to prevent folic acid deficiency.

Pediatric population:
A more appropriate dosage form should be used for young children.

Treatment of megaloblastic anemia due to folate deficiency:
In children aged 1-18 years: 5 mg (1 tablet) daily for 4 months; 5 mg (1 tablet) every 1 to 7 days for maintenance therapy.

Geriatric population:
No special dose adjustment is required for elderly patients.

4.3. Contraindications

- Known hypersensitivity to the active substance or any of the excipients
- Long-term folate therapy is contraindicated in any patient with untreated cobalamin deficiency. Cobalamin deficiency may present as other cobalamin deficiencies, including patients with untreated pernicious anemia or patients who are lifelong vegetarians. In elderly patients, a cobalamin absorption test should be performed before starting long-term folate therapy. Administration of folate to these patients for 3 months or more has accelerated cobalamin neuropathy. No harmful effects are seen with short-term folate use.
- Folic acid should never be given alone in Addisonian pernicious anemia and other vitamin B12 deficiency conditions because it may precipitate development of subacute combined degeneration of the spinal cord (except during pregnancy and lactation, doses higher than 0.4 mg/day should not be recommended until pernicious anemia is proven to be absent. Folic acid may improve hematologic abnormalities, but neurologic problems may be irreversibly increased).
- Folic acid should not be used in malignant diseases unless megaloblastic anemia due to folate deficiency is a major complication.

4.4. Special warnings and precautions for use

Folic acid alone is not an appropriate treatment for pernicious anemia and other megaloblastic anemias with vitamin B12 deficiency. This is because folic acid doses above 0.1 g per day reduce hematologic symptoms but mask neurologic symptoms. In order to prevent this, it must be given together with adequate doses of vitamin B12.

Caution should be exercised in the use of folic acid in patients with tumor formation receiving folate antagonist therapy. It may reduce the effect of chemotherapeutics.

Antibiotics may interfere with the microbiological assay for serum and erythrocyte folic acid concentrations and may cause falsely low results.

FOLAS contains lactose monohydrate. Patients with rare hereditary galactose intolerance, Lapp lactose insufficiency or glucose-galactose malabsorption problems should not use this medicine.

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

The need for folic acid may increase in patients on long-term use of adrenocorticoids, analgesics, anticonvulsants, hydantoin or estrogens.

When folic acid supplements are given to treat folic acid deficiency caused by the use of antiepileptics (phenytoin, phenobarbital and primidone), serum antiepileptic levels may decrease and may lead to decreased seizure control in some patients.

Methotrexate, primethamine, triamterene or trimethoprim act as folate antagonists by inhibiting dihydrofolate reductase.

Sulfonamides, including sulfasalazine, inhibit folate absorption, so folic acid requirement may be increased in patients taking sulfasalazine.

Chloramphenicol antagonizes the action of folic acid. Co-trimoxazole may interfere with folate metabolism.

Additional informations on special populations:
No data available.

Pediatric population:
No data available.

4.6. Fertility, pregnancy and lactation

General advise
Pregnancy category: A

Women of childbearing potential/Birth control (contraception):
Well-conducted epidemiologic studies have not shown that FOLAS has adverse effects on pregnancy or on the health of the fetus/newborn child.

FOLAS can be used during pregnancy.

Pregnancy:
No problems have been reported if the normal daily requirement is taken. Folic acid supplements are generally useful.

Non-drug-induced folic acid deficiency or abnormal folate metabolism is associated with the occurrence of birth defects and some neural tube defects. Folate deficiency or disturbances in folic acid metabolism induced by drugs such as anticonvulsants and some antineoplastics in early pregnancy result in congenital anomalies. Deficiency of the vitamin or its metabolites may also be implicated in spontaneous abortion and intrauterine growth retardation in some cases.

Breast-feeding:
Folic acid is actively excreted in breast milk. Folate accumulation in milk outweighs maternal folate requirements. Folic acid levels in colostrum are relatively low, but vitamin concentrations increase as lactation progresses. No adverse effects have been observed in breastfed infants whose mothers took folic acid.

Reproductive ability / Fertility:
Not available.

4.7. Effects on ability to drive and use machines
It is not known whether it has any effect on the ability to drive and use machines.

4.8. Undesirable effects
Folic acid is generally well tolerated.

Very common (≥1/10); common (≥1/100 to <1/10); not common (≥1/1.000 to <1/100); rare (≥1/10.000 to <1/1.000); very rare (<1/10.000), not known (cannot be estimated based on available data).

Immune system disorders
Rare: Allergic reactions, erythema, rash, pruritus, urticaria, dyspnea and anaphylactic reactions (including shock).

Nervous system disorders
Changes in sleep patterns, irritable mood, psychotic reactions have been reported in some people.
These reactions disappear after discontinuation of the drug.

Gastrointestinal disorders
Rare: Anorexia, nausea, abdominal distension and flatulence.

4.9. Overdose and treatment.
No special procedure or antidote is required.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamic properties
Pharmacotherapeutic group: Antianemic preparations, Folic acid and its derivatives
ATC code: B03BB01

Folic acid belongs to the vitamin B group. It is essential for nucleoprotein synthesis and maintenance of normal erythropoiesis. In particular, it stimulates the production of red blood cells, white blood cells and platelets in some people with megaloblastic anemia.

5.2. Pharmacokinetic properties
General characteristics

Absorption:
Approximately all dietary folic acid is absorbed from the gastrointestinal tract (mainly from the proximal part of the small intestine) and distributed to body tissues, even in the presence of malabsorption due to tropical sprue. Dietary folate is reported to have about half the bioavailability of crystalline folic acid. Naturally occurring folate polyglutamates are largely deconjugated in the intestine and reduced by the enzyme dihydrofolate reductase to form 5-methyltetrahydrofolate (5MTHF). Therapeutically administered folic acid enters the portal circulation largely unchanged because it is a poor substrate for reduction by dihydrofolate reductases.

Distribution:
Folic acid is distributed through the portal circulation. 5MTHF, which is derived from naturally occurring folate, is widely bound to plasma proteins. Folate is mainly stored in the liver. It is also actively concentrated in the cerebrospinal fluid. It is excreted in breast milk.

Biotransformation:
Folic acid (in the presence of ascorbic acid) is converted to its active metabolite (tetrahydrofolic acid) by dihydrofolate reductase in the liver and plasma. There is an enterohepatic circulation for folate.

Elimination:
Up to 4 - 5 micrograms per day is excreted in the urine. In proportion to higher doses, the amount above the daily requirement is excreted unchanged. Folic acid is removed by hemodialysis.

Linearity / Non-linearity:
No data available.

5.3. Preclinical safety data
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6. PHARMACEUTICAL PARTICULARS
6.1. List of excipients
Lactose monohydrate
Pregelatinized starch
Sodium starch glycolate
Colloidal silicon dioxide
Talc
Magnesium stearate

6.2. Incompatibilities
It does not show physical or chemical incompatibility in the package in which it is contained.

6.3. Shelf life
24 months

6.4. Special precautions for storage

Store at room temperature below 25°C, in its original packaging, protected from light.

This product and/or its packaging should not be used if it contains any defects.

6.5. Nature and contents of container

Each box contains 50 tablets. Tablets are presented in transparent PVC/PVDC/Aluminum foil blister packaging.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

2023/235

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21.06.2023

Date of latest renewal:

10. DATE OF REVISION OF THE TEXT