For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory.

Cyanocobalamin Ferrous Fumarate and Folic Acid Capsules

Autrin® Haematinic Capsules

1. NAME OF THE MEDICINAL PRODUCT

Autrin

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard gelatin capsule contains:

Cyanocobalamin (Vitamin B12) I. P.	15 mcg
(As Cyanocobalamin I. P. 0.1% in Gelatin)	
Ferrous Fumarate I. P.	300 mg
(equivalent to 98.6 mg of elemental iron)	
Folic Acid I. P.	1.5 mg
Appropriate overages of vitamins added	

Vitamins for Therapeutic Use

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsules

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Autrin is indicated in the treatment and maintenance of

- Iron deficiency anaemia
- Megaloblastic anaemia of nutritional origin
- Anaemia of pregnancy

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Licensed User - Pfizer Limited, India

- Other anaemias deemed responsive to the ingredients.

4.2 Posology and Method of Administration

As directed by the physician.

4.3 Contraindications

Autrin is contraindicated in patients with proven allergy to any ingredient.

- Contraindicated in patients with hemochromatosis, hemosiderosis and hemoglobinopathies.
- Contraindicated in patients with active peptic ulcer, repeated blood transfusions, regional enteritis and ulcerative colitis.

4.4 Special Warnings and Special Precautions for Use

Autrin alone should not be relied upon for correction of isolated Vitamin B12 and/or folic acid deficiency and specific therapy should be instituted in these cases.

Cases not responding satisfactorily to Autrin should be investigated for sites of continued blood loss or other causes of apparent haematinic failure.

4.5 Interaction with Other Medicinal Products and Other Forms of Interaction

Iron chelates with concomitantly administered tetracyclines, and absorption of both agents may be impaired, allow an interval of 2-3 hours if treatment with both drugs is necessary.

Absorption of iron may be reduced in the presence of antacids and proton pump inhibitors which reduce stomach acid. Iron absorption may also be reduced in the presence of food (e.g. tea, coffee, wholegrain cereals, eggs and milk), neomycin and cholestyramine. Bicarbonates, carbonates, oxalates, or phosphates, may impair the absorption of iron by the formation of insoluble complexes.

Iron absorption may be reduced with calcium, oral magnesium salts and other mineral supplements, zinc and trientine. If treatment with both iron and trientine is necessary a suitable interval is advised.

Iron absorption may be increased by ascorbic or citric acid.

The response to iron may be delayed in patients receiving systemic chloramphenicol. Chloramphenicol delays plasma clearance of iron and incorporation of iron into red blood cells by interfering with erythropoiesis.

The hypotensive effect of methyldopa is reduced by iron.

Concomitant use of iron and dimercaprol should be avoided as toxic complexes may form.

Iron reduces the absorption of fluoroquinolones, levodopa, carbidopa, entacapone, bisphosphonates, penicillamine, thyroid hormones such as levothyroxine (give at least 2 hours apart), mycophenolate, cefdinir and zinc. Iron possibly reduces the absorption of eltrombopag (give at least 4 hours apart).

Serum levels of anticonvulsant drugs may be reduced by the co-administration of folate e.g. folic acid possibly reduces the plasma concentration of phenobarbital, phenytoin and primidone.

Concomitant use of folic acid with raltitrexed should be avoided.

Absorption of folic acid is possibly reduced by sulfasalazine.

4.6 Fertility, Pregnancy and Lactation

Pregnancy

Ferrous fumarate can be used during pregnancy if clinically indicated. Controlled studies in women fail to demonstrate a risk to the fetus in the first trimester (and there is no evidence of a risk in later trimesters), and the possibility of fetal harm appears remote with folic acid. Vitamin B12 should be given in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

No adverse effects of ferrous fumarate have been shown in breastfed infants of treated mothers. Ferrous fumarate can be used during breast feeding if clinically indicated. Folic acid is excreted in breast milk. No adverse effects have been observed in breast-fed infants whose mothers were receiving folic acid. Vitamin B12 is excreted in breast milk. Vitamin B12 should be given in lactation only if the potential benefit justifies the potential risk to the fetus.

4.7 Effects on Ability to Drive and Use Machine

Does not affect ability to drive and to use machinery

4.8 Undesirable Effects

As with all orally administered iron salts, Autrin may cause gastric irritation, dyspepsia, etc. in sensitive individuals. Allergies to folic acid have been reported.

4.9 Overdose

Acute poisoning in young children is especially dangerous.

Symptoms:

Abdominal pain, vomiting and diarrhoea. Cardiovascular collapse with coma may follow. In severe cases, deterioration may occur involving diffuse vascular congestion, pulmonary edema, convulsions, anuria, hypothermia, severe shock and metabolic acidosis.

Treatment:

Includes inducing vomiting and gastric lavage. In severe cases, parenteral desferrioxamine may be used.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Ferrous fumarate provides elemental iron in a well-tolerated form specifically to meet iron requirements of red blood cell formation and building of tissue iron stores. Dosage of iron recommended for prevention and control of iron deficiency anemia in pregnant women is 100 mg elemental iron.

Cyanocobalamin and folic acid are haemopoietic factors, which participate in formation of nuclei of newly forming red blood cells.

Folic acid is a member of Vitamin B group. Folic acid is reduced in the body to tetrahydrofolate which is a coenzyme for various metabolic processes including the synthesis of purine and pyrimidine nucleotides and hence in the synthesis of DNA. Deficiency of folic acid can result in megaloblastic anemia.

Cyanocobalamin is Vitamin B12. It is required for conversion of homocystine and methionine. When conversion is deficient, folate metabolism is disturbed causing a defect in DNA synthesis and a failure of maturation of megaloblasts. Cyanocobalamin thus assists the action of folic acid in forming nucleic acid.

All these three ingredients have been added with the sole aim of assisting haemopoesis. Along with ferrous fumarate, Cyanocobalamin and folic acid are added since each of these causes anemia in deficient states.

5.2 Pharmacokinetic Properties

Ferrous fumarate:

Absorption of iron takes place mainly in the duodenum and jejunum; aided by gastric acid secretion. Absorption depends on the amount of stored iron in the body. Absorption is higher when stored iron is low. Ferrous iron passes through the GI mucosal cells, binds to transferrin and is then transported to the bone marrow and incorporated into hemoglobin.

Ferrous fumarate is mainly excreted through the faeces and desquamation of cells e.g. skin, hair or gastrointestinal mucosa.

Folic acid:
Folic acid is rapidly absorbed, mainly from the proximal part of the small intestine. Folic acid is extensively bound to plasma proteins. Folic acid is largely metabolized in the liver and mainly excreted in the urine.

Vitamin B12:
The absorption of Vitamin B12 from the gut is dependent upon the glycoprotein intrinsic factor. Vitamin B12 is transported rapidly into the blood bound to protein, known as transcobalamin. Vitamin B12 is stored in the liver, excreted in the bile and undergoes enterohepatic recycling.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Light Liquid Paraffin IP, Magnesium Stearate IP, Dibasic Calcium Phosphate Anhydrous IP, Corn Starch IP.

Approved colours used in empty capsule shell: -Quinolline Yellow, Carmoisine, Brilliant blue and Titanium Dioxide I. P.

6.2 Incompatibilities

None stated.

6.3 Shelf-life

18 Months

6.4 Special Precautions for Storage

Store at a temperature not exceeding 30°C.

Keep out of the reach of children.

6.5 Nature and Contents of Container

Blister pack of 30 capsules

6.6 Instructions for Use and Handling

None specific