For the use of a registered medical practitioner or a laboratory only

PREXAN™

(Ferrous Fumarate, Elemental Iron, Folic acid, Cyanocobalamin, Copper & Sodioum Docusate)

COMPOSITION

Each film-coated tablet contains:
Ferrous Fumarate I.P. equivalent to
Elemental Iron ……..…… 60 mg
Folic Acid I.P. ……..…… 1 mg
Cyanocobalamin I.P. (As Gelatin Triturate) ……. 7.5 mcg
Copper Gluconate U.S.P. equivalent to
Elemental Copper ……..…… 1 mg
Docusate Sodium I.P. ……..... 50 mg
Colours: Lake of Ponceau 4R & Titanium Dioxide I.P.
Appropriate overages of vitamins added to compensate for loss on storage.

DESCRIPTION

Hemopoiesis requires adequate supplies of minerals likes iron and copper, vitamins like folic acid, vitamin B_{12}: and various hematopoietic growth factors. PREXAN is a haematinic that contains iron salts (ferrous fumarate), folic acid, cyanocobalamin and docusate sodium. Iron salt (e,g, ferrous fumarate) are primarily required for the prophylaxis and treatment of iron deficiency anaemia.

CLINICAL PHARMACOLOGY

PHARMACODYNAMICS

Ferrous Fumarate

Iron, an essential mineral, is a component of hemoglobin, myoglobin and number of enzymes (eg. cytochromes, catalase, perioxidase. The total body content of iron is = 50 mg /kg is men (3.5 g in the average 70 kg man) and 37 mg / kg in woman. Iron is primarily stored as hemosiderin or aggregated ferritin, found in the reticuloendothelial cells of the liver, spleen and bone marrow. Appoximately two-thirds of the total body iron is in the circulating red blood cell mass in hemoglobins, the major factor in oxygen transport, iron is necessary for effective erythropoiesis, is a cofactor of several essential enzymes, including cytochromes, all of which are involved in electron transport. The ferrous from of inorganic iron is more readily absorbed.

Folic Acid

Folic acid, after conversion to 5, 6, 7, 8 – tetrahydrofolate polyglumate, functions as a coenzyme in single carbon unit transfer. Thus in purine synthesis it donates format (-CHO) to from carbon 2 and 8 of the purine nucleus. In pyrimidine synthesis it donates the 5- methyl groups and this methyl is transferred to homocysteine to from methioninc. Sources of single units include format, serine and histidine.

Cyanocobalamin

Cyanocobalamin is readily converted into the coenzyme forms which, as methylcobalamin is concerned with conversion of hemocysteine to methionine and as deoxyadenosylcobalamin in the conversion of methylmalonyl - CoA to succinyl - CoA. The active coenzymes, methylcobalamin and 5-deoxyadenosylcobalamin, are essential for growth and replication.

Copper

Copper as an essential trace element exists in the diet, it is needed to absorb and utilize iron. The oxidation of ferrous iron into ferric state is carried by ceruloplasmin. In the gut, copper deficiency can affect iron absorption through modulating the activity of hephacstin - a milti-copper oxidase required for optimal iron export from enterocytes. This depletion of copper could impair iron absorption.

Docusate Sofium

Docusate is an anionic surfactant (i.e., a surface-active agent). It lowers the surface tension at the oil-water interface of the faeces, allowing water and lipids to penetrate the stool. This help to hydrate and soften the faecal material, facilitating natural defecation. At usual recommended doses, docusate exhibits little intrinsic stimulatory actions and thus cannot be considered a laxative. Docusate has a delayed onset of action, with softening of the stool becoming apparent after 1-3 days of therapy.

PHARMACOKINETICS:

Ferrous Fumarate

Absorption/ Distribution – The average dietary intake of iron is 12 to 20 mg / day for male and 8 to 15 mg / day for females: however, only = 10% of this iron is absorbed (1 to 2 mg / day) in individuals with adequate iron stores. Absorption is enhance (20% to 30%) when storage iron is depleted or when erthropolesis at an increased rate. Iron is primarily absorbed from the duodenum and upper jejunum by an active transport mechanism. The ferrous salt from is absorbed three times more readily than the ferric from. The common ferrous salt (sulfate, gluconate, Fumarate) are absorbed almost on a milligram- for –milligram basis but differ in the content of elemental iron. Sustained-release or enteric-coated preparations reduce the amount of available iron: absorption from these dose influence the amount of iron absorbed. The amount of iron absorbed increases progressively with larger doses: however, the percentage absorbed decreases. Food can decrease the absorption of iron by 40% to 66%: however, gastric intolerance may often necessitate administering the drug with food.

Excretion – Iron is transported via the blood and bound to transferring. The daily loss of iron from urine, sweat and sloughing of intestinal mucosal cells amounts to = 0.5 to 1 mg in healthy men. In menstruating women, = 1 to 2 mg is the normal daily loss.

Folic Acid

About 70 -80% of a 2 mg oral dose of folic acid is absorbed. Larger doses are probably equally well absorbed. It is distributed into plasma and extracellular fluid. In plasma, folate is bound weakly to albumin. About 70% of small doses of folate (about 1 mg) are retained and rest excreted into urine. With larger doses most is excreted into the urine. With a 5 mg dose of folat, urinary excretion will be complete in about 5 hours. There is an entrohepatic circulation of

folate. The retained folate is taken into cells and reduced by dihydrofolate reductase to terahydrofolate. Folic acid is a relatively poor substrate for folate reduction, the normal subtract being dihydrofolate. Folic acid itself doses not occur in natural materials, it is entirely a pharmacological form of the compound.
Once reduced, folate has additional glutamic acid residues added a folate pentaglutamate being the dominant intracellular analogue. These polyglutamates are the active coenzymes. Folate enters breast milk which may be beneficial to the infant.

Cyanocobalamin
Vitamin B_{12} is irregularly absorbed from the distal intestine following oral administration. Dietary vitamin B_{12} is protein bound must be split by proteolysis and gastric acid before absorption. In the stomach, free vitamin B_{12} is attacked to intrinsic factor, intrinsic factor a glycoprotein secreted by the gastric mucosa, is necessary for active absorption of the vitamin from the GI trace. The vitamin B_{12} intrinsic factor complex passes into the intestine, where much to the complex is transiently retained at specific receptor sites. In the wall of the lower ileum before the vitamin B_{12} portion is absorbed into systemic circulation. Vitamin B_{12} is distributed into liver, bone marrow, and other tissues, including the placenta At birth, blood concentration of vitamin B_{12} in neonates is 3-5 times that in the mother, vitamin B_{12} is distributed into the milk of nursing women in concentration. The daily turnover rate of vitaminB_{12} is 0.05-0.2% of total body stores, and may range from 0.4-8mcg, depending on the size of the storage pool.

Copper:
The average daily intake of copper in the US is about 1mg copper with the primary source being the diet. The bioavailability of copper from the diet is about 65- 70% depending on a variety of factors including chemical form, interaction with other metals, and dietary components. The serum copper concentration ranges up to approximately 1.5mg/ L in healthy person. The biological half-life of copper from the diet is 13-33 days with biliary excretion being the major route of elimination.

Docusate Sofium
Docusate calcium is administrated orally: docusate sodium is administrated orally and rectally. Because docusate salts are minimally absorbed and exert their effects locally; standard pharmacokinetic parameters do not apply. Some systemic absorption occurs in the jejunum and duodenum, but the extent of this is subsequently excreted in the bile. Pharmacodynamically, faecal softening begins 1-3 days following initiation of oral docusate administration.

INDICATIONS
Iron deficiency: For the prevention and treatment of iron deficiency and iron deficiency anemia's.
Iron supplement: As a dietary supplement for iron.

WARNING AND PRECAUTIONS
Foli acid alone is improper therapy in the treatment of pernicious anemia and other megaloblastic anemias where B12 is deficient.

Anemia is a manifestation that requires appropriate investigation to determine its cause or causes. No single regime fits all cases and the status of the patient observed in follow-up is the final criterion for adequacy of therapy. Periodic clinical and laboratory studies are considered essential. Blood examinations including hemoglobin and hematocrit should be done at the usual intervals to make certain that therapy is adequate. Use with care in the presence of peptic ulcers, regional enteritis, and ulcerative colitis. Folic acid, especially in doses over 0.1 mg daily may obscure pernicious anemia, in that hematologic remission can occur while neurological manifestations remain progressive.

Chronic iron intake: Individuals with normal iron balance should not take iron chronically.

Drug / Food interactions:
Eggs and milk inhibit iron absorption. Coffee and tea consumed with a meal or 1 hour after a meal may significantly inhibit the absorption of dietary iron: clinical significance has been determined. Administration of calcium and iron supplements with food can reduce ferrous sulfate absorption by one - third. If combined iron and calcium supplementation is required, iron absorption is not decreased if calcium carbonate is used and the supplements are taken between meals.

Renal Impairment
Iron supplementation is required in virtually all patients with chronic renal failure who are under going hemodialysis, particularly those receiving epoetin alfa, because of the blood losses associated with hemodialysis and the increased demands for iron induced by epoetin alfa-induced erythropoiesis.

Hepatic Impairment
In animal studies, iron and its inorganic salts have generally not caused cancer, except when implanted increased risk for hepatocellilar carcinoma occurs with development of liver cirrhosis from iron overload.

DRUG INTERACTIONS
Cimetidine: The decrease of gastric acid caused by cimetidine may decrease the absorption of non-heme iron, concurrent use is not recommended. Iron supplements should be taken at least 2 hours before cimetine.

Fluroquinoloes: Iron may reduce the absorption of fluoroquinoloes by chelation, resulting in lower serum and urine concentration of fluoroquinolones: fluoroquinolones should be taken at least 2 hour after iron supplements.

Pancreatin or Pancrealipase: Concurrent use of / Pancreatin or Pncrealipase / with iron supplements decrease iron absorption.

Tetracyclines: Concurrent use with iron reduces absorbability and resultant therapeutic effects of oral tetracyclines: patients should be advised to take iron supplements 2 hours after letracycline.

Concurrent use / of whole – grain breads and cereals (contain phytic acid and dietary fiber) / with iron may decrease iron absorption because or the formation of loss soluble or insoluble complexes; iron supplements should not be taken within 1 hour before or 2 hour after ingestion.

UNDESIRABLE EFFECTES

GI irritation; nausea; vomiting; constipation; diarrhea.

Iron-containing liquids may temporarily stain the teeth. Dilute the liquid to reduce this possibility. When iron-containing drops are given to given to infants, the membrane covering the teeth may darken.

Gastrointestinal disturbances (anorexia, nausea, diarrhea, constipation, heartburn and vomiting) occur occasionally, but are usually mild and may subside with continuation of therapy. Reducing the dose and administering it with meals will minimize these effects in the sensitive patient.

Increasing fiber in the diet can relieve constipation. Iron may turn stools black. This is a harmless effect that is a result of unabsorbed iron. Although the absorption of iron is best when taken between meals, giving Prexan after meals may diminish occasional G.I. disturbances. Prexan is best absorbed when taken at bedtime.

Allergic sensitizations have been reported following both oral and parenteral administration of folic acid.

OVERDOSAGE

Symptoms:

The oral lethal dose of elemental iron is =200 to 250 mg/ kg however considerably less has been fatal. Symptoms may present when 30 to 60 mg / kg is ingested. Acute poisoning will produce symptoms in four stages:

1. Within 1 to 6 hour; Lethargy, nausea, vomiting, abdominal pain, tarry stools, fever, leukocytosis; hyperglycemia; dyspnea; coma.
2. If not immediately fatal, symptoms may subside for= 24hours.
3. Symptoms return 12 to 48 hours after ingestion and may include. Diffuse vascular congestion; pulmonary edema; shock; metabolic acidosis; convulsions; anuria; hyperthermia; death.
4. If patient survives, in 2 to 6 weeks after ingestion, pyloric or antral stenosis, hepatic cirrhosis and CNB damage may be seen.

Treatment

Maintain proper airway, respiration and circulation. If the patient is a candidate for emesis, include with syrup with Ipecac; follow with gastric lavage using tepid water or 1% to 5% sodium bicarbonate. Systemic chelation therapy with deferoxamine is generally recomanded for patients with serum iron levels greater than the total binding capacity (63mcmol; 3.5 mg / L); IM therapy may suffice, but severe poisoning (e,g, shock, coma) may require IV administration. Oral use of

deferoxamine is treatment for shock, convulsions, acidosis and renal failure may be necessary. Treatment includes usual supportive measures

DOSAGE AND ADMINISTRATION
The usual prophylactic dose in adults suggested by WHO is about 60 mg of elemental iron daily. The usual adult treatment dose is sufficient of these salts to supply about 100 to 200 mg of supplemental iron daily.

1-2 capsules per day depending on the nutritional status of the patients or as directed by the physician.

Iron Supplementation:
Pregnancy – 15 to 30 mg elemental iron daily (not taken with meals) should be adequate to meet the daily requirement of the last 2 trimesters.

PREGANANCY & LACTATION:
Category B
No physiological system of elimination exists for iron, and it can accumulate in the body to toxic amounts; however, small amounts are lost daily in breast milk (1.1 to 1.4 mg / day).

Geriatric Use
Some geriatric patients may require a larger than usual daily ingestion of bioavailable iron to correct an iron deficiency because their ability to absorb iron has been diminished by reduced gastric secretions and achlorhydria.

STOREAGE
Store in a dry place below 30°c.
KEEP OUT REACH OF CHILDREN

EXPIRY DATE
Two years from the date of manufacturing.

PACKAGING INFORMATION
Blister pack of 30 Tablets

MARKETED BY
TORRENT PHARMACEUTICALS LTD.
Torrent House, Off Ashram Road,
Ahmedabad-380 009, INDIA