For the use only of Registered Medical Practitioners or a Hospital or a Laboratory

FERSOLATE® CM

Tablets of Ferrous Sulphate with Copper and Manganese

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sugar coated tablet contains:

Dried Ferrous Sulphate IP : 0.195 g
Copper Sulphate BP : 2.6 mg
Manganese Sulphate Monohydrate BP : 2.0 mg

Colour: Red Oxide of Iron.

PHARMACEUTICAL FORM

Tablets for oral administration.

CLINICAL PARTICULARS

Therapeutic Indications

For prophylaxis of iron deficiency anaemia.

For supplementation of iron, copper and manganese in deficiency states such as in:
- unbalanced dietary intake
- pregnancy and lactation
- old age
- infections
- convalescence
- adolescence

Posology and Method of Administration

Route of Administration

For oral administration.

The tablets should not be sucked, chewed or kept in the mouth, but swallowed whole with water.

Tablets should be taken before meals or during meals, depending on gastrointestinal tolerance

Adults

One tablet (containing 63.375 mg elemental iron) daily.

Children

This presentation is not recommended.
Elderly

As for adults.

Renal impairment

Caution should be exercised in patients with renal disorders.

Hepatic impairment

Caution should be exercised in patients with liver diseases (see Section Contraindications and Special Warnings and Special Precautions for Use).

Contraindications

Hypersensitivity to FERSOLUTE CM and its ingredients; haemosiderosis and haemochromatosis; active peptic ulcer; repeated blood transfusion; haemolytic anaemia. In Wilsons disease (hepatolenticular degeneration), a disease of abnormal copper accumulation, liver failure. Oral and parenteral iron preparations should not be used concomitantly.

Patients with rare hereditary problems of fructose intolerance, glucose- galactose malabsorption or sucrase- isomaltase insufficiency should not take FERSOLUTE CM.

Special Warnings and Special Precautions for Use

Patients post-gastrectomy have poor absorption of iron. Caution is advised when prescribing iron preparations to individuals with history of peptic ulcer, and inflammatory bowel disease, including regional enteritis and ulcerative colitis. Care should be taken in patients with intestinal strictures or diverticulae.

Dental caries is a definite risk following long term use of FERSOLUTE CM.

These tablets contain sugar and should be administered with care to patients with diabetes.

Patients suffering from iron overload are particularly susceptible to infection. Treatment of iron overload should be with caution.

Some patients with end-stage liver disease have been found to accumulate manganese in their basal ganglia. It is thought that manganese may play a role in the hepatic encephalopathy in those with liver failure. Manganese is eliminated primarily through the bile and hepatic dysfunction leads to depressed manganese excretion. Therefore, FERSOLUTE CM is contraindicated in patients with liver failure.

Due to the risk of mouth ulcerations and tooth discoloration, tablets should not be sucked, chewed or kept in the mouth, but swallowed whole with water.

Interaction with Other Medicaments and Other Forms of Interaction

Antacids and mineral supplements

Compounds containing calcium, magnesium (including antacids and mineral supplements), bicarbonates, carbonates, oxalates or phosphates may impair the absorption of iron. Administration of iron preparations with such compounds should be separated by at least 2 hours.
Concomitant administration of gastric acid neutralising agents, calcium preparations (carbonates or phosphates) and magnesium as well as cholestyramine, may reduce manganese absorption.

Concomitantly taken zinc supplements reduce the absorption of copper and iron. Iron preparations and zinc preparations can reduce the absorption of each other. Magnesium supplements may decrease absorption of manganese if taken concomitantly.

**Thyroid hormone**

Ferrous sulphate reduces the absorption of levothyroxine and so should be taken at least 2 hours apart.

**Trientine**

Absorption of oral iron preparations is reduced by trientine. Administration should be separated by at least 2 hours.

**Penicillamine**

Oral iron preparations can reduce the absorption of penicillamine. Also the absorption of iron is impaired by penicillamine.

Concomitant use of penicillamine and copper can cause decreased absorption of both substances.

**Antibacterials**

Iron and tetracyclines reduce the absorption of each other when administered concomitantly. Administration of iron preparations and tetracyclines should be separated by 2 to 3 hours. Iron may reduce the absorption of quinolones. Administration of iron preparations and quinolones should be separated by at least 2 hours. Chloramphenicol delays plasma clearance of iron, incorporation into red blood cells by interfering with erythropoiesis.

Tetracyclines reduce the absorption of manganese if taken concomitantly.

**Biphosphonates**

The absorption of biphosphonates is reduced when taken concurrently with iron preparations. Administration should be separated by at least 2 hours.

**Cholestyramine**

Absorption of iron is impaired by cholestyramine.

**Dimercaprol**

Concomitant administration of oral iron preparations and dimercaprol should be avoided.

**Dopaminergics**

Oral iron preparations may reduce the absorption of dopaminergics such as co-careldopa, entacapone and levodopa.
**Food Products**

Absorption of iron is impaired by tea, eggs or milk.

**Methyldopa**

Oral iron preparations may antagonise the antihypertensive effect of methyldopa.

**Mycophenolate mofetil**

Oral iron preparations significantly reduce the absorption of mycophenolate mofetil.

**Laxatives**

Magnesium containing laxatives may decrease the absorption of manganese if taken concomitantly.

**Vitamin C**

Vitamin C supplementation of 1,500 mg daily caused the activity of copper transporting protein ceruloplasmin to decline. Vitamin C supplementation of 600 mg daily also caused a decline in ceruloplasmin, but copper absorption was not impaired.

**Pregnancy and lactation**

During pregnancy and lactation, use of FERSOLATE CM should always be under the direction of a physician. Use of any drug during the first trimester of pregnancy should be avoided if possible.

Prophylaxis of iron deficiency during the second and third trimester of pregnancy is justified.

**Effects on Ability to Drive and Use Machines**

None known.

**Undesirable Effects**

Post-marketing:

The following ADRs have been reported during post-marketing surveillance. The frequency of these reactions is considered not known (cannot be estimated from the available data).

**Ferrous Sulphate**

**Gastro-intestinal disorders**

Abdominal pain, nausea and vomiting (these are usually dose related), constipation, diarrhoea and dark stools. Contact irritation can occur with tablets containing ferrous sulfate resulting in erosion or ulceration, particularly if they become lodged in the upper gastrointestinal tract.

**Mouth ulceration**

* in the context of incorrect administration, when the tablets are chewed, sucked or kept in mouth.

Elderly patients and patients with deglutition disorders may also be at risk of oesophageal lesions or of bronchial necrosis, in case of false route.
Allergic reactions have been reported.

**Copper**

*Not known:* Nausea, vomiting, epigastric pain and diarrhea.

**Manganese**

Oral manganese may be neurotoxic in those with liver failure. Manganese may accumulate in the basal ganglia of those with liver failure and may exacerbate hepatic encephalopathy and/or cause Parkinson’s disease like symptoms.

Manganese madness with symptoms similar to those of Parkinson’s disease has been reported.

**Overdose**

Iron overdosage is an acute emergency requiring urgent medical attention. An acute intake of 75mg/kg of elemental iron is considered extremely dangerous in young children. Serum iron levels should be monitored.

Symptoms and signs include abdominal pain, diarrhoea, nausea, vomiting (haematemesis is a possibility) and hyperglycaemia within 1-2 hours, followed by cardiovascular collapse and coma in some patients. Recovery follows this phase and in some patients this continues. In others deterioration occurs after about 15 hours characterised by pulmonary oedema, convulsions, renal failure, shock, metabolic acidosis, hypotension, tachycardia, coagulopathy and/or hypoglycaemia. There is a potential for gastrointestinal obstruction to occur weeks after iron ingestion, as a delayed effect.

**Treatment**

Treatment consists of supportive and symptomatic measures. Vomiting should be induced if patient presents early and gastric lavage should be considered using a solution of desferrioxamine. Parenteral injection of 2 gm desferrioxamine should be given IV or IM and 5gm of desferrioxamine in 50-100ml of fluid may also be left in the stomach. Recovery may be complicated by long term effects such as hepatic necrosis.

Specific antidotes D-penicillamine, BAL (Dimercaprol) for copper may be administered.

**PHARMACOLOGICAL PROPERTIES**

**Pharmacodynamic Properties**

**Iron**

Ferrous Sulphate contains iron. Most of the iron in the body is present as haemoglobin. The remainder is present in the storage forms ferritin or haemosiderin, in the reticuloendothelial system or as myoglobin with smaller amounts occurring in haem-containing enzymes or in plasma bound to transferrin.

**Copper**

It is essential for synthesis of hemoglobin, formation of bone and myelin, for the activity of certain enzymes, such as cytochrome oxidases (tissue oxidation).
Manganese

It is a co-factor in many enzyme reactions, which involve phosphorylation and synthesis of cholesterol and fatty acids.

Pharmacokinetic Properties

Iron

Iron is absorbed mainly in the small intestine, but can be absorbed along the entire length of the alimentary canal. It is absorbed most easily in the ferrous state, passing into and through the mucosal cells directly into the blood stream where it is immediately attached to transferrin.

Copper

Copper is principally absorbed in the small intestine, A small amount of copper is absorbed in the stomach. Copper appears to be absorbed by both active and passive processes. At low and moderate intakes of copper, it appears to be absorbed by saturable active transport mechanism. At higher copper intakes the active transport mechanism becomes saturated and copper is absorbed by passive diffusion. The absorption efficiency of copper ranges from 15% to 97% and appears to depend on the level of dietary copper intake. As dietary copper increases, the fractional absorption of copper decreases.

Following absorption from the small intestine, copper is transported in the bile primarily bound to albumin. Copper is mainly taken up by the liver and heart where it is principally incorporated into ceruloplasmin. Copper containing ceruloplasmin is released from the liver into the blood and delivered to cells containing ceruloplasmin receptors. Copper containing ceruloplasmin binds to these receptors and release, copper into the cell. The major route of copper excretion is via bile into the gastrointestinal tract.

Manganese

There is scant information on the pharmacokinetics of manganese in humans. The efficiency of absorption (fractional absorption) of ingested manganese appears to be low, about 5%. Absorption efficiency appears to decrease as dietary intake of manganese increases. It increases with low dietary intake of manganese. Absorbed manganese is excreted primarily via the biliary route. Very little manganese is excreted in the urine.

Preclinical Safety Data

There are no relevant data available.

PHARMACEUTICAL PARTICULARS

List of excipients

Gum Acacia, Sucrose, Paraffin liquid, Tartaric acid, Stearic acid, Methylene chloride, Methyl hydroxybenzoate, Propyl hydroxybenzoate, Starch Maize, Magnesium stearate, Heavy Kaolin, Talc purified, Iron oxide red GSK1, Gelatin, Calcium carbonate, Dextrin 200, Paraffin hard, Trichloroethelene
Incompatibilities

There are no relevant data available.

Shelf life

24 months.

The expiry date is indicated on the label and packaging.

Special Precautions for Storage

Keep in a cool place.

Keep out of reach of children.

Nature and Specification of Container

Amber glass bottle in a carton.

Instructions for Use / Handling

There are no special requirements for use or handling of this product.

For further information please contact:
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Adapted from


2. Theragran M NCDS version 01 dated 11 June 2012.

3. PDR/Micromedex for Copper and PDR/Martindale for Manganese.