SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Ferrograd Folic Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Dried Ferrous sulfate 325 mg (elemental iron 105 mg)
Folic acid BP 350 micrograms

3 PHARMACEUTICAL FORM

Prolonged release, film coated tablets.
Circular, biconvex, two layered, red and yellow tablet.

4 CLINICAL PARTICULARS

4.1. Therapeutic indications

Prevention and treatment of iron deficiency anaemia of pregnancy.

Prophylaxis of megaloblastic anaemia of pregnancy.

4.2 Posology and method of administration

Adults including the elderly

1 tablet daily throughout pregnancy and the first month of the puerperium. Take before food.

Children

Not recommended for children under 12 years.

Method of 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.

4.3. Contraindications

Megaloblastic anaemia due to primary vitamin B_{12} deficiency.

Ferrograd Folic is contraindicated in patients with pernicious anaemia.

Intestinal diverticular disease or any intestinal obstruction.

Iron preparations are contra-indicated in patients with haemochromatosis and haemosiderosis.

Iron is contra-indicated in patients receiving repeated blood transfusions.

Oral iron preparations are contra-indicated when used concomitantly with parenteral iron therapy.

Ferrograd Folic is contraindicated in the rare instance of hypersensitivity to folic acid.

4.4. Special warnings and precautions for use

Ferrograd Folic tablets should be kept out of children's reach. Acute iron poisoning occurs rarely in adults, however it could happen if children swallow this medication.

The label will state ‘Important warning: Contains iron. Keep out of the reach and sight of children, as overdose may be fatal’. This will appear on the front of the pack within a rectangle in which there is no other information.

The controlled release tablet and its inert plastic matrix may cause a safety hazard in some elderly or other patients suffering from delayed intestinal transit.

Pernicious anaemia is rare in women of childbearing age and is less likely in pregnancy as vitamin B_{12} deficiency reduces fertility. However, folic acid, at the recommended dosage, may obscure the neurological manifestations of pernicious anaemia.

Iron preparations colour the faeces black, which may interfere with tests used for detection of occult blood in the stools. The guaiac test occasionally yields false positive tests for blood.

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

Aspiration of iron sulfate tablets can cause necrosis of the bronchial mucosa which may result in coughing, haemoptysis, bronchostenosis and/or pulmonary infection (even if aspiration happened days to months before these symptoms occurred). Elderly patients and patients who have difficulties swallowing should only be treated with iron sulfate tablets after a careful evaluation of the individual patient's risk of aspiration. Alternative formulations should be considered. Patients should seek medical attention in case of suspected aspiration.

This product contains the excipient lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

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

Iron interacts with tetracyclines, magnesium trisilicate, trientine and zinc salts and absorption of all of these agents may be impaired.

Iron inhibits the absorption of tetracyclines from the gastrointestinal tract and tetracycline inhibits the absorption of iron. If both drugs must be given, tetracycline should be administered three hours after or two hours before oral iron supplements.

Concurrent administration of oral iron preparations with antacids, calcium supplements (calcium carbonate or phosphate), tea, coffee, eggs, food or medications containing bicarbonates, carbonate, oxalates or phosphates, milk or milk products, wholegrain breads and cereals and dietary fibre, may decrease iron absorption. Therefore, oral iron preparations should not be taken within one hour before or two hours after ingestion of such items.

Concurrent administration of oral iron preparations may interfere with the oral absorption of some quinolone anti-infective agents (e.g. ciprofloxacin, norfioxacin, ofloxacin), resulting in decreased serum and urine concentrations of the quinolones. Therefore, oral iron preparations should not be ingested with or within two hours of a dose of an oral quinolone.

Iron can decrease gastrointestinal absorption of penicillamines. Therefore, administration should be at least two hours apart if both drugs must be co-administered.

Chloramphemcol may delay response to iron therapy.

4.6. Pregnancy and lactation

Ferrograd Folic is indicated for prevention and treatment of iron deficiency anaemia of pregnancy, and prophylaxis of megaloblastic anaemia of pregnancy.

Folic acid is excreted in breast milk.

4.7. Effects on ability to drive and use machines

None.

4.8. Undesirable effects

Side-effects reported are similar to those associated with conventional oral iron preparations, i.e. nausea, vomiting, abdominal pain or discomfort, blackening of stools, diarrhoea and/or constipation, but the incidence of side-effects is less owing to the prolonged release nature of the formulation.

Isolated cases of allergic reaction have been reported ranging from rash to anaphylaxis. Allergy is more common in those people who are allergic to aspirin.

Allergic sensitisation has been reported following both oral and parenteral administration of folic acid.

Bronchial stenosis (see section 4.4)

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).

Gastrointestinal disorders:

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.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9. Overdose

Symptoms: Initial symptoms of iron overdosage include nausea, vomiting, diarrhoea, abdominal pain, haematemesis, rectal bleeding, lethargy and circulatory collapse. Hyperglycaemia and metabolic acidosis may also occur. The prolonged release characteristic may delay excessive absorption of iron, and thus allow more time for counter measures to be implemented. However, initial symptoms of overdosage may be absent due to the prolonged release

formulation. Therefore, if overdosage is suspected, treatment should be implemented immediately. In severe cases, after a latent phase, relapse may occur after 24-48 hours, manifested by hypotension, coma and hepatocellular necrosis and renal failure.

Treatment: The following steps are recommended to minimise or prevent further absorption of the medication:

Children:

1. Administer an emetic such as syrup of ipecacuanha.

2. Emesis should be followed by gastric lavage with desferrioxamine solution (2g/l). This should then be followed by the instillation of desferrioxamine 5 g in 50-100 ml water, to be retained in the stomach. Inducing diarrhoea in children may be dangerous and should not be undertaken in young children. Keep the patient under constant surveillance to detect possible aspiration of vomitus - maintain suction apparatus and standby emergency oxygen in case of need.

3. Unleached tablets are radio-opaque. Therefore, an abdominal x-ray should be taken to determine the number of tablets retained in the stomach following emesis and gastric lavage.

4. Severe poisoning: in the presence of shock and/or coma with high serum iron levels (serum iron >90 μmol/l) immediate supportive measures plus i.v. infusion of desferrioxamine should be instituted. Desferrioxamine 15 mg/kg body weight should be administered every hour by slow i.v. infusion to a maximum 80 mg/kg/24 hours. Warning: hypotension may occur if the infusion rate is too rapid.

5. Less severe poisoning: i.m. desferrioxamine 1 g 4-6 hourly is recommended.

6. Serum iron levels should be monitored throughout.

Adults:

1. Administer an emetic.

2. Gastric lavage may be necessary to remove drug already released into the stomach. This should be undertaken using desferrioxamine solution (2g/l). Desferrioxamine 5 g in 50-100 ml water should be introduced into the stomach following gastric emptying. Keep the patient under constant surveillance to detect possible aspiration of vomitus; maintain suction apparatus and standby emergency oxygen in case of need.

3. Unleached tablets are radio-opaque. Therefore, an abdominal x-ray of the patient should be taken to determine the number of tablets retained in the stomach following emesis and gastric lavage. The risk/benefit ratio of x-raying pregnant women must be carefully weighed but should be avoided if possible.

4. A drink of mannitol or sorbitol should be given to induce small bowel emptying.

5. Severe poisoning: in the presence of shock and/or coma with high serum iron levels (>142 μmol/l) immediate supportive measures plus i.v. infusion of desferrioxamine should be instituted. The recommended dose of desferrioxamine is 5 mg/kg/h by slow i.v. infusion up to a maximum of 80 mg/kg/24 hours. Warning: hypotension may occur if the infusion rate is too rapid.

6. Less severe poisoning: i.m. desferrioxamine 50 mg/kg up to a maximum dose of 4 g should be given.

7. Serum iron levels should be monitored throughout.

5 PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Folic acid requirements in pregnancy can be met with supplements of between 300 and 400 micrograms daily. Without such supplements, folate deficiency may develop, leading to megaloblastic anaemia with attendant obstetric risks. Doses over 400 micrograms may mask undiagnosed vitamin B_{12} deficiency. In the extremely unlikely event of this condition occurring in a pregnant woman, the safe prophylactic dose is considered to be 350 micrograms.

Iron provided by Ferrograd Folic aids haemoglobin regeneration. Once haemoglobin returns to normal, continuing iron therapy for 3 months will help replenish the iron stores in the body.

5.2. Pharmacokinetic properties

The Gradumet® device allows controlled release of ferrous sulphate over a number of hours and reduces gastro-intestinal intolerance. The device consists of an inert plastic matrix, honeycombed by thousands of narrow passages which contain ferrous sulphate together with a water soluble channelling agent. As the tablet passes down the gastro-intestinal tract the iron is leached out. The spent matrix is finally excreted in the stools.

Iron is found in the body principally as haemoglobin. Storage in the form of ferritin occurs in the liver, spleen, and bone marrow. Concentrations of plasma iron and the total iron-binding capacity of the plasma vary greatly in different physiological conditions and disease states.

Folic acid and iron are absorbed in the proximal small intestine, particularly the duodenum. Folic acid is absorbed maximally and rapidly at this site, and iron is absorbed in a descending gradient from the duodenum distally.

After absorption, folic acid is rapidly converted into its metabolically active forms. Approximately two-thirds is bound to plasma protein. Half of the folic acid stored in the body is found in the liver. Folic acid is also concentrated in spinal fluid.

5.3. Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Tablet core:
Methylacrylate methylmethacrylate copolymer,
Magnesium stearate,
Povidone,
Polyethylene glycol 8000,
Colloidal silicon dioxide,
Lactose,
Sucrose,
Acacia powder,
Maize starch,

Tablet coat:
Cellulose acetate phthalate,
Propylene glycol,
Sorbitan monooleate,
Castor oil,
Titanium dioxide
Dye Red Ponceau 4R Lake (E124).

6.2. Incompatibilities

None.

6.3. Shelf life

3 years.

6.4. Special precautions for storage

Store in a cool dry place at or below 25°C.

6.5. Nature and contents of container

Carton containing 30 (3x10) tablets in a blister (OP), and a sample blister of 4 tablets.

6.6. Instructions for use, handling and disposal

None.

7. MARKETING AUTHORISATION HOLDER

Via F.lli Cervi, 8
I-27010 Valle Salimbene (PV)
Italy

8. MARKETING AUTHORISATION NUMBER

PL 16250/0004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/06/2004

10 DATE OF REVISION OF THE TEXT

05/10/2018