Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ferrograd Folic 325mg/0.35mg Prolonged release Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains:
Dried Ferrous Sulphate 325 mg (elemental iron 105 mg)
Folic Acid 0.35mg (350 micrograms)

Excipients with known effect:
Each tablet contains 2 mg Dye Red Ponceau 4R Lake (E124), 30 mg sucrose and 257 mg lactose monohydrate.

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Prolonged release tablet.
Circular biconvex, 2 layered, red and yellow film-coated tablet

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

For the prophylaxis and treatment of iron and folic acid deficiencies and if used in pregnancy should be used after the first 13 weeks of pregnancy only.

4.2 Posology and method of administration

Adults: The recommended dosage is one tablet daily before food.

Children: Not applicable.

Elderly: As for adults. The sustained release tablet and its inert plastic matrix may cause a safety hazard in some elderly or other patients suffering from delayed intestinal transit.

* Medical advice should be sought if symptoms do not improve after four weeks of use of this product as these symptoms may reflect on underlying disease process.

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

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Ferrograd Folic should not be used in the presence of megablastic anaemia due to primary vitamin B12 deficiency or any undiagnosed anaemia.

Use in patients with intestinal diverticular or any intestinal obstruction.

• Individuals with haemochromatosis and iron overload syndromes.

Patients with rare hereditary problems of fructose intolerance, galactose intolerance, the Lapp lactase deficiency, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.4 Special warnings and precautions for use

The label will state “Important warning: Contains iron. Keep out of 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. Caution is advised in individuals with a family history of haemochromatosis or iron overload syndromes. It should be noted these conditions may be under diagnosed. Overdose may be fatal.

As with all iron preparations, this product should be used with caution in patients with haemochromatosis, haemolytic anaemia or haemoglobinopathies. The sustained release tablet and its inert plastic matrix may cause a safety hazard in patients suffering from delayed intestinal transit. There may also be a further delay in release of the iron.

Ferrograd Folic contains the colour E124, which may cause allergic type reactions including asthma; allergy is more common in those people who are allergic to aspirin.

This product should only be used for the prevention and treatment of iron deficiency anaemia diagnosed by laboratory testing under the supervision of a medical doctor.

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.

4.5 Interaction with other medicinal products and other forms of interaction

Iron salts diminish the absorption of tetracyclines. Tetracycline antibiotics should be taken at least 2 hours before or 3 hours after taking Ferrograd Folic.

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

Thyroid hormones: Oral iron reduces the absorption of levothyroxine (thyroxine) thus should be given at least 2 hours apart.

Iron salts may reduce the bioavailability of methyldopa, the absorption of levodopa and penicillamine may also be reduced.

The absorption of iron salts is decreased in the presence of antacids and preparations containing zinc, calcium, phosphorus or when taken with tea, coffee, milk, eggs, wholegrain cereals and dietary fibre. Therefore, oral iron preparations should not be taken within one hour before or two hours after ingestion of these products. Iron absorption may be increased by ascorbic or citric acid.

Serum levels of anticonvulsant drugs may be reduced by the co-administration of folate e.g. Ferrograd Folic may possibly reduce the plasma concentration of phenobarabital, phenytoin and primidone. Absorption of Ferrograd Folic is possibly reduced also by sulfasalazine.

4.6 Fertility, pregnancy and lactation

Ferrograd Folic is indicated for the prophylaxis of iron and folic acid deficiencies, after the first 13 weeks of pregnancy. It should only be taken during the first 13 weeks of pregnancy in consultation with a doctor. However, administration of drugs during the first trimester of pregnancy requires careful assessment of potential risks versus benefits to be gained.

Iron is excreted in breast milk so consult your doctor if you intend breast feeding.

4.7 Effects on ability to drive and use machines

Ferrograd Folic has no influence on the ability to drive and use machines.

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, diarrhea and/or constipation, but the incidence of side-effects is less owing to the controlled release nature of the formulation. Haematemesis and ileus have been reported.

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).

Immune system disorders:
Anaphylactic reaction

Respiratory, thoracic and mediastinal disorders:
Bronchial stenosis (see section 4.4)

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

4.9 Overdose

Initial symptoms of iron overdosage include nausea, vomiting, abdominal pain, diarrhoea, haematemesis and rectal bleeding. However, following a massive overdosage of Ferrograd Folic, these initial symptoms may be absent due to its sustained release characteristics. Therefore if overdosage is suspected treatment should not be delayed by the absence
of symptoms.

A latent phase followed by a relapse 24 – 48 hours after ingestion manifest by hypotension, coma and hepatocellular necrosis may occur.

Treatment: The ingested Gradumet matrix cannot be readily aspirated through a stomach tube and there is no known chemical that will dissolve the gradumet without harming gastric mucosa. Accordingly when overdosage is discovered early, the following procedure is recommended.

1. Administer an emetic by stomach tube.

2. Withdraw the stomach tube and wait for the patient to vomit.

3. Keep the patient under constant surveillance to detect possible aspiration of vomitus; maintain suction apparatus and standby emergency oxygen in case of need.

4. Examine the vomitus for returned Gradumet tablets.

5. Administer a saline purgative. By the time toxic signs have appeared, Gradumet tablets are in most cases past the pylorus so that emesis is of no value. Gastric lavage may be considered to remove amounts of the drug already released in the stomach. A saline purgative should then be given to speed the Gradumet tablets along the alimentary canal so as to minimise or prevent further absorption of the medication.

6. The use of an iron-chelating agent such as oral desferrioxamine should be considered. In severe cases parenteral desferrioxamine may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Iron provided by Ferrograd Folic aids haemoglobin regeneration. Once haemoglobin returns to normal, continuing with iron supplementation for three months will help replenish the iron stores within the body.

5.2 Pharmacokinetic properties

The Gradumet device allows sustained release of the active ingredient over a number of hours, which increases iron utilisation and reduces gastrointestinal intolerance. The device consists of an inert plastic matrix honeycombed by thousands of narrow passages, which contain active drug together with a water-soluble channelling agent. As the tablet passes down the gastrointestinal tract, the iron is leached out. The spent matrix is finally excreted in the stools.

Oral iron is absorbed better when administered between meals; however, conventional iron preparations often cause gastric irritation when taken on an empty stomach. Studies with Gradumet iron have indicated that relatively little of the iron is released into the stomach, the major proportion being released in the upper intestinal tract. Thus the possibility of gastric irritation is minimised when iron is administered in the Gradumet form in comparison with
conventional oral iron preparations. Controlled release iron, therefore, is beneficial to patients who have a demonstrated intolerance to oral iron preparations.

After absorption, folic acid is rapidly converted into its metabolically active forms. Approximately 2/3 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 the spinal fluid.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to information contained in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet Core

Methylacrylate methylmethacrylate copolymer
Magnesium stearate
Macrogol 8000
Dye red ponceau 4R lake
(E124) Titanium dioxide
(E171) Colloidal Anhydrous
Silica
Povidone
Sucrose (Sugar)
Lactose
Monohydrate
Acacia powder
Maize starch

Film coating

Cellacefate
Macrogol 8000
Propylene glycol

Sorbitan Oleate
Castor oil, virgin

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25^{o}C. Store in the original package in order to protect from light. Keep out of reach and sight of children.

6.5 Nature and contents of container

Carton containing 30 (3 x 10) tablets in an AL/PVC blister.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Teofarma S.R.L
Valle Salimbene (PV)
Via F. LLI Cervi
8 CAP 27010
Italy

8 MARKETING AUTHORISATION NUMBER

PA1235/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 01 April 1980

Date of last renewal: 01 April 2010

10 DATE OF REVISION OF THE TEXT

January 2019