SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

<Trade Name> <Strength> film-coated tablets

1. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 200 mg dried ferrous sulfate, equivalent to 65 mg ferrous iron.

Excipient(s) with known effect:

<Regarding the approval>

For a full list of excipients, see section 6.1.

1. PHARMACEUTICAL FORM

Film-coated tablets

<Regarding the approval>

1. CLINICAL PARTICULARS
   1. Therapeutic indications

For the prevention and treatment of iron-deficiency anaemias.

* 1. Posology and method of administration

Posology

Each 200 mg ferrous sulfate tablet is equivalent to 65mg of ferrous iron.

*Adults:*

Treatment: 130-195 mg ferrous iron (2-3 tablets) daily in divided doses. Prophylaxis: 65 mg ferrous iron (1 tablet) daily.

*Elderly:*

The usual adult dose can be administered (see section 4.4).

*Children 6-12 years:*

Treatment: Children weighing over 22 kg - one tablet daily.

Children weighing over 44 kg - one tablet twice daily.

Children weighing over 66 kg – one tablet three times daily.

*Children under 6 years or weighing less than 22 kg:*

Not recommended.

*Renal impairment:*

The usual adult dose can be administered. However, patients with chronic renal failure on haemodialysis may require iv iron therapy.

*Hepatic impairment*

There are no adequate data for specific dosing recommendations in the case of impaired liver function.

Method 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.

The duration of treatment depends on the type and severity of the disease. Basically, iron therapy is necessary to achieve a therapy success over a period of at least 8 weeks. After normalisation of the Hb value, the iron deposit should be treated for 6-8 weeks to replenish the iron deposit.

The efficacy of the treatment should be monitored by blood tests

* 1. Contraindications
* Hypersensitivity to the active substance or any of the other excipients listed in section 6.1.
* Paroxysmal nocturnal haemoglobinuria.
* Haemosiderosis and haemochromatosis
* Active peptic ulcer
* Patients receiving repeated blood transfusions
* Regional enteritis and ulcerative colitis
* Haemolytic anaemia
* Oral and parenteral iron preparations should not be used concomitantly.
  1. Special warnings and precautions for use

Some post-gastrectomy patients show poor absorption of iron.

Administer with caution in patients with haemoglobinopathies, iron storage or iron-absorption diseases, existing gastrointestinal disease.

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. Duration of treatment should generally not exceed 3 months after correction of anaemia.

Dental caries is a definite risk following long term treatment with this product.

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

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

Co-existing deficiency of vitamin B12 or folic acid should be ruled out since combined deficiency produces microcytic blood film.

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.

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

The label will state

‘Important warning: Contains iron. Keep out of the sight and reach 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.

* 1. Interaction with other medicinal products and other forms of interaction

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.

The absorption of ciprofloxacin, levofloxacin, norfloxacin and ofloxacin may be reduced by oral iron.

*Quinolones:* Iron may reduce the absorption of quinolones. Administration of iron preparations and quinolones should be separated by at least 2 hours.

Chloramphenicol delays plasma iron clearance, incorporation of iron into red blood cells and interferes with erythropoiesis.

*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.

*Bisphosphonates:* The absorption of bisphosphonates 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. Absorption of iron salts is enhanced by ascorbic acid and meat.

*Methyldopa:* Oral iron preparations may antagonise the antihypertensive effect of methyldopa.

*Mycophenolate mofetil:* Oral iron preparations significantly reduce the absorption of mycophenolate mofetil.

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

*Thyroid hormone:* Ferrous sulfate reduces the absorption of levothyroxine and so should be taken at least 2 hours apart.

*Trientine:* The absorption of oral iron preparations is reduced by trientine. Administration should be separated by at least 2 hours.

*Zinc:* Iron preparations and zinc preparations can reduce the absorption of each other.

* 1. Fertility, pregnancy and lactation

Pregnancy

There are no controlled studies on the use of Ferrous Sulfate in pregnancy. Reports on adverse effects after administration of oral iron preparations in therapeutic doses for the treatment of anaemia during pregnancy are not yet known.

Use of any drug during the first trimester of pregnancy should be avoided if possible. Thus, administration of iron during the first trimester however requires evidence of iron deficiency. Prophylaxis of iron deficiency during the remainder of pregnancy is justified.

Treatment with Ferrous Sulfate should only be done after a careful benefit-risk assessment and the higher dosage of 3 tablets per day should not be prescribed over a longer period of time. Iron preparations are insufficiently tested for reproductive toxicity in animal studies (see section 5.3).

Breast-feeding

Ferrous (II) salts are excreted in human milk, but at therapeutic doses of Ferrous Sulfate no effects on the breastfed newborn /infant are anticipated. Ferrous Sulfate should be prescribed during breastfeeding only after careful risk-benefit assessment.

Fertility

Ferrous sulfate can have a potential effect on fertility. Animal studies are insufficient for potential effects on fertility (see section 5.3).

* 1. Effects on ability to drive and use machines

Probably there is no effect, but there are no data available.

* 1. Undesirable effects

The frequency details for the side effects mentioned in the following vary considerably in the underlying literature. Significant studies with sufficient patient populations are not available.

The following frequencies are used for the assessment of side effects:

Very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/ 1,000, <1/100), rare (≥1/10,000, <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

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| Immune system disorders   * Allergic reactions have been reported.   Respiratory, thoracic and mediastinal disorders   * Not known: Bronchial stenosis (see section 4.4)   Gastro-intestinal disorders   * Very common: nausea, epigastric or abdominal pain * Common: A darkening of the stool due to the resulting black iron sulphide is a phenomenon which is frequently observed, but completely safe, after the administration of oral iron preparations.; diarrhoea, vomiting (these are usually dose related). * Uncommon: Occasionally, gastrointestinal disorders can occur, such as anorexia and constipation. Constipation can be remedied by balancing nutrition. * Not known: Mouth ulceration and teeth discoloration (reversible)\*   \* 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, bronchial necrosis in case of false route.  Skin and subcutaneous tissue disorders   * Common: Rash * Rare: In rare cases, hypersensitivity reactions (e.g., skin symptoms) may occur. Contact irritation can occur with ferrous sulfate tablets resulting in erosion or ulceration, particularly if they become lodged in the upper gastrointestinal tract. |

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 Health Product Vigilance Center; HPVC, Thai FDA.

* 1. Overdose

To avoid the risk of possible overdosing of iron, special care should be taken if dietary or other iron salt supplements are used. These should be taken into account when dosing ferrous Sulfate.

If there is a history of inflammation of the gastro-intestinal tract or peptic ulcer, the benefits of the treatment should be carefully weighed up against the risk of making gastro-intestinal conditions worse.

*Adults:* Ingestion of 20 mg/kg elemental iron is potentially toxic and 200- 250 mg/kg is potentially fatal.

*Paediatric population:* As little as 20 mg/kg elemental iron is enough to lead to symptoms of toxicity.

Symptoms

Acute iron overdosage can be divided into four stages:

In the first phase, which occurs up to 6 hours after oral ingestion, gastrointestinal toxicity, notably vomiting and diarrhoea, predominates. Other effects may include cardiovascular disorders such as hypotension and tachycardia, metabolic changes including acidosis and hyperglycaemia, and CNS depression ranging from lethargy to coma. Patients with only mild to moderate poisoning do not generally pass this first phase.

The second phase may occur at 6-24 hours after ingestion and is characterised by a temporary remission or clinical stabilisation.

In the third phase gastrointestinal toxicity recurs together with shock, metabolic acidosis, convulsions, coma, hepatic necrosis and jaundice, hypoglycaemia, coagulation disorders, oliguria or renal failure, and pulmonary oedema.

The fourth phase may occur several weeks after ingestion and is characterised by gastrointestinal obstruction and possibly late hepatic damage.

Overdosage of ferrous salts is particularly dangerous to young children.

Poisoning with oral iron preparations in most cases affects children. In small children 400 mg can already cause serious intoxication.

Serious toxic effects after intake of 60 mg/kg body weight.

Locally, iron leads to serious corrosion of the gastrointestinal tract, and the reabsorbed iron leads to serious damage in the nervous system and the liver.

Management

Treatment consists of gastric lavage followed by the introduction of 5 g desferrioxamine into the stomach.

Serum iron levels should be monitored and in severe cases iv desferrioxamine should be given together with supportive and symptomatic measures as required.

Gastric lavage with 5% sodium bicarbonate and saline cathartics (e.g. sodium sulfate 30 g for adults); milk and eggs with 5 g bismuth carbonate every hour as demulcents.

Blood or plasma transfusion for shock, oxygen for respiratory embarrassment.

Chelating agents (e.g. disodium calcium edetate) may be tried (500 mg/500 ml by continuous iv infusion).

Dimercaprol should not be used since it forms a toxic complex with iron. Desferrioxamine is a specific iron chelating agent and severe acute poisoning in infants should always be treated with desferrioxamine at a dose of 90 mg/kg IM followed by 15 mg/kg per hour iv until the serum iron is within the plasma binding capacity.

1. PHARMACOLOGICAL PROPERTIES
   1. Pharmacodynamic properties

*Pharmacotherapeutic group:* anti-anaemic preparations

ATC code: B03A A07

Iron plays a central role in the metabolic process as a component of the red blood dye (haemoglobin) and numerous enzymes (for example cytochrome oxidase, peroxidase, catalase). Due to iron deficiency, almost all cell functions are impaired, in particular the processes associated with high oxygen demand, e.g. growth processes. However, the amounts of iron absorbed with the food are relatively small so that larger losses are hardly to be compensated for, but an oral substitution is required.

The daily requirement for men, women after the menopause, and children is about 0.5 - 1 mg of iron, for younger women and adolescents about 1 - 2 mg, for pregnant women about 2 - 5 mg, and for infants about 0.5 - 1.5 mg. With an average absorption rate of 10%, at least 10 times the amount daily is to be administered orally, in order to cover the requirement. In the adult organism, about 2.5 g iron is to be found as haemoglobin iron, 1.5 g as storage iron, less than 0.4 g as myoglobin iron, less than 0.1 g as haem-containing enzymes and about 4 mg in plasma bound to transferrin.

* 1. Pharmacokinetic properties

Iron is absorbed by the mucosal transferrin, preferably in the upper small intestinal region, depending on the needs. Iron (II) salts are more ionized there and more bioavailable than iron (III) salts. The resorption rate of the dietary iron is on the average 5-15% (average 0.5-1.5 mg daily); it usually increases with exhausted iron reserves and decreases with increasing amount of iron. In plasma, iron is bound by plasma transferrin, excess iron is stored as ferritin or hemosiderin in the reticuloendothelial system and mobilised as required.

Ferrous Sulfate should be taken 1 hour before or possibly between meals as food can affect absorption. Reduced availability for resorption results from the formation of sparingly soluble iron compounds with phytates (cereals), phosphates (milk), oxalates (spinach, rhubarb), tannin (tea).

* 1. Preclinical safety data

Animal experiments with Ferrous Sulfate, which are carried out according to the current standard, are not available for the possible effects of iron salts on fertility, embryofetal and postnatal development.

There is no evidence of potential mutagenicity of iron in mammalian cells in vivo.

There are no long-term studies on tumour-producing potential.

1. PHARMACEUTICAL PARTICULARS
   1. List of excipients

<Regarding the approval>

* 1. Incompatibilities

<Regarding the approval>

* 1. Shelf life

<Regarding the approval>

* 1. Special precautions for storage

<Regarding the approval>

* 1. Nature and contents of container

<Regarding the approval>

* 1. Special precautions for disposal

<Regarding the approval>

1. MARKETING AUTHORISATION HOLDER

<Regarding the approval>

1. MARKETING AUTHORISATION NUMBER(S)

<Regarding the approval>

1. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Regarding the approval>

1. DATE OF REVISION OF THE TEXT1

<Regarding the approval>