SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF MEDICINAL PRODUCT
FERIFER 100 mg/5 ml oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5 ml solution (1 spoon) contains,

Active substance:

Iron (III) (as in iron polymaltose complex)	100 mg

Excipients:

Sorbitol (70%) (E420)	1500 mg
Methyl paraben sodium (E219)	7.5 mg
Propyl paraben sodium (E217)	2.5 mg

For a full list of excipients, see Section 6.1.

3. PHARMACEUTICAL FORM
Oral solution
Red brownish, clear solution having aromatic odor (vanilla)

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
It is used in treatment and prophylaxis of all iron deficiencies which are originated from various causes, and iron deficiency anemia; in iron supplementation treatment in pregnancy, lactation and in children

During pregnancy, folic acid supplementation should also be considered with iron supplementation.

4.2 Posology and method of administration
Posology/frequency and duration of administration

Children (> 12 years-old), adult and elder
Latent iron deficiency: 1/2 - 1 spoon a day (50 – 100 mg)
Severe iron deficiency: 1 spoon, twice and three times a day (200 – 300 mg)

The duration of treatment depends on iron metabolism (reduced intake, increased needs and pathologic loss) and normalizing erythrocyte level. Average 3-5 months are needed to achieve normal blood levels for treatment of significant iron deficiency. The duration of treatment for latent iron deficiency 1-2 months.

It is needed to use 1 spoon a day for 2 – 3 months to fill up body reserve after the Hb concentration returns to normal.

Method of administration:
It is directly taken orally within a spoon.

Additional information on special populations
Renal/Hepatic failure: It should not be used in severe liver disease.

Pediatric population: In children under 12 years of age, there is not enough data to recommend a dosage regimen for routine use at this time.

Geriatric population: Use in elderly people is the same as the use in adults.

4.3. Contraindications
It should not be administered in cases with hypersensitivity against any substances within the content, hemochromatosis, hemosiderosis, aplastic or hemolytic or sideroblastic anemia, thalassemia, chronic pancreatitis, hepatic cirrhosis, and in individuals who have frequent blood transfusions

4.4. Special warnings and precautions for use
It should be kept out of reach of children.

Diseases which may cause iron deficiency or iron deficiency anemia should be identified, and treated appropriately.

There is no special warning for tolerance or addiction risks. Other than continuous bleeding, menorrhagia, and pregnancy, treatment should not extend longer than 6 months.

In children, accidental intake of iron containing products may cause fatal toxicity.
Keep out of reach of children.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose-isomaltose deficiency should not take this medicine since it contains sorbitol.

It contains methyl paraben sodium and propyl paraben sodium, which may cause delayed allergic reaction.

Color of stool may be darkened because of iron content

Use in the following conditions should be carefully evaluated:
Alcoholism, hepatitis, active infectious conditions, inflammatory conditions of the intestinal system such as enteritis, colitis, diverticulitis, and ulcerative colitis, pancreatitis and peptic ulcer

4.5 Interaction with other medicinal products and other forms of interaction

Iron (III) in Iron (III) Hydroxide Polymaltose Complex is not expected to show ionic interaction with foods and medicines, because it is included in the complex. Treatment may be unresponsive when iron (II) salts are taken with antacids such as magnesium trisilicate and carbonate. Mild and egg may decrease iron absorption. If it is to be taken with tetracycline, cholestyramine antacids, penicillamine and oral gold compounds, it should be given with an interval of several hours. Concomitant use with salicylates, phenylbutazone, and oxyphenbutazone may cause irritation of intestinal mucosa. Benzidine test may be positive during the iron treatment. It should not be taken together with tea, coffee, and milk. It should be used carefully in individuals with intestinal tumors.

When medicines containing levothyroxine are taken simultaneously with FERIFER, the absorption is impaired. Therefore, the two medicines should be taken at least 2 hours apart.

4.6. Pregnancy and lactation
Pregnancy category: A

• Despite this pregnancy category, the physician's final decision on whether to use the drug or not; It should be given by making a detailed benefit-risk assessment according to the gestational week, existing/detected disease of the pregnant woman and other characteristics.

• Although the risk categories help the health professionals about the potential risk of the drug in pregnancy, the evaluation of the physician is essential.

Women with childbearing capacity / Birth control (Contraception)
It has no negative effects on women with childbearing capacity / Birth control (Contraception).

Pregnancy
Controlled trials performed with drugs of this category in women indicated no harm on fetus when drugs are used in the first trimester of pregnancy. There is no evidence that the drug is harmful in later trimesters. It has been concluded in conducted studies that iron requirements are increased in pregnant women. These are the most reliable drugs in pregnancy. It can be used in pregnancy under a physician supervision.

Lactation
Lactating mothers can use this drug under a physician supervision.

4.7 Effects on ability to drive and use of machines
There is no negative effects on ability to drive and use of machines.

4.8 Undesirable effects
The specified undesirable effects are classified according to the following rule:
Very common (≥ 1/10); common (≥ 1/100 to ≤ 1/10); uncommon (≥ 1/1000 to ≤ 1/100); rare (≥ 1/10000 to ≤ 1/1000); very rare (≤ 1/10.000); unknown (Frequency cannot be estimated from the available data).

Immune system disorders:
Rare: Allergic reactions

Gastrointestinal disorders:
Rare: Fresh blood in the stools
Common: Diarrhea, nausea, epigastric pain, constipation, vomiting, dark colored stools

Kidney and urinary tract disorders:
Uncommon: Dark colored urine

Irritation, which is the cause of these symptoms, may be prevented by decreasing the dose or taking the drug after the meals.

4.9 Overdose
Although no intoxication case related to overdose has been reported, Desferrioxamine or Calcium disodium EDTA use is recommended.

Urgent and Supporting Cure:
If necessary, provide basic and advanced life support. As necrotizing gastroenteritis can cause blood and fluid loss, hypotension and shock; intravenous fluid support, hypotension, and shock treatment should be applied. Liquid electrolyte imbalance, if any should be corrected, convulsion should be treated.

Specific antidote and drug:
Chelation therapy is proceeded with deferoxamine in the following conditions:
1. Patients with severe clinical data (lethargy, acidosis, hypovolemia, abdominal pain)
2. All patients with recurrent mild symptoms (vomiting more than once, soft stools more than once)
3. All patients who have serum iron level from 350 to 500 micrograms/dl with and without symptoms
4. Patients with radiopaque iron particles on abdominal x-ray despite gastric lavage

Deferoxamine is given by intravenous at 15 mg/kg/hr rate. The total amount of drug per day should not exceed 6 g. The treatment can be maintained for 24 hours according to the patient's condition. Acute respiratory distress syndrome (ARDS) can develop if it is used for a long time. Hypotension, rash, redness of the face or even the possibility of anaphylaxis during infusion should be kept in mind. Treatment with deferoxamine can also be used in pregnancy.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Iron (III) polymaltose
ATC Code: B03AB05

Polynuclear Iron (III) hydroxide nuclei are surrounded by superficially non-covalently bound polymaltose molecules.

Iron (III) Hydroxide Polymaltose Complex is stable, and it does not release ionic iron under physiological conditions. In polynuclear nuclei, iron is bound to physiologically formed structures resembling ferritin, and it is actively absorbed.

Iron absorption is performed by iron binding receptors in the gastrointestinal fluids and on the superficial epithelium via “competitive binding switch” mechanism.

Iron (III) Hydroxide Polymaltose Complex does not have prooxidative properties like iron (II) salts. Tendency to oxidation of lipoproteins such as VLDL and LDL is decreased.

5.2 Pharmacokinetic properties:

General characteristics
Absorption
Clinical trials performed by using ‘‘Twin-isotope’’ technique have shown that iron absorption ratio, namely ratio of iron entering into hemoglobin, is increased as the level of iron deficiency is increased. In other words, there is a positive correlation between severity of iron deficiency and the ratio of iron absorbed. If the body does not require iron, absorption is not possible whatever

the amount of the dose given. Iron absorption occurs mainly in the duodenum and jejunum. Unabsorbed iron is eliminated with feces via intestines.

Elimination
Iron in the body is eliminated via gastrointestinal tract and exfoliating epithelial cells from the skin. Only 1 mg iron is eliminated via bile and urinary tract. Additionally, women lose iron during menstruation.

5.3. Preclinical safety data
No LD_{50} value for FERIFER has been defined after the oral administration of 2000 mg iron per kilogram of body weight in animal trials conducted on white mice and rats.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients
Sorbitol (%70) (E420)
Methyl paraben sodium (E219)
Propyl paraben sodium (E217)
Citric acid
Vanilla flavor
Glycerin
Propylene glycol
Deionized water

6.2. Incompatibilities
There is no evidence that FERIFER 100 mg/5 ml Spoon Containing Oral Solution has an incompatibility with any drug or substance

6.3. Shelf life
24 months

6.4 Special precautions for storage
Store at room temperature below 25ºC.

6.5 Nature and contents of container
FERIFER is presented as 10, 20, 28 or 30 disposable spoons in 5 ml PET spoons, each of which is covered by aluminum folio. Each presentations are also packed in the PVC separators

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling
Any unused product or waste material should be disposed of in accordance with “Directive on Control of Medical Waste” and “Directive on the Control of Packaging and Packaging Waste”.

7. MARKETING AUTHORIZATION HOLDER

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8. MARKETING AUTHORIZATION NUMBER(S)
238/56

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION
Date of the first authorization: 22.12.2011
Date of the renewal of the authorization: 05.11.2018

10. DATE OF REVISION OF THE TEXT
23.03.2020