SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
FERIFER 50 mg/ml oral drops

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1 ml (20 drops) contains;

Active substance:
It contains 147 mg of iron III hydroxide polymaltose complex, equivalent to 50 mg of iron.

Excipients:

Sucrose	50 mg
Methyl paraben (E218)	1.8 mg
Propyl paraben (E216)	0.2 mg
Sodium hydroxide	0.133 mg

For the full list of excipients, see section 6.1.

3.PHARMACEUTICAL FORM
Drops
Red-brown aromatic odor solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications
It is used for the treatment of iron deficiency of various origins and treatment and prevention of iron deficiency anemia; treatment of iron deficiency during pregnancy, lactation and childhood.

Folic acid supplementation in combination with iron should be considered during pregnancy.

4.2 Posology and method of administration
Posology:
FERIFER dose is 100-200 mg for adults, 100 mg for children over 12 years, 50-100 mg for children between 1-12 years; in patients up to 1 years of age, it should be started at 5 drops daily and titrated up to 20 drops. In newborns it is used at 1 drop per kg.

Frequency and duration of administration:
Unless otherwise recommended by the doctor, it is administered at the doses indicated below.

Newborns: 1 drop/kg/day
Up to age 1: Start at 5 drops/day, can be titrated up to 20 drops/day in divided doses.
1-12 years: 1-2 times 20 drops (50-100 mg) daily
Over 12 years: 2 times 20 drops (100 mg) daily
Adults: 1-2 times 40 drops (100-200 mg) daily

It should be used for the period of time recommended by the doctor.
Treatment should be continued for at least another month to fill iron stores after iron deficiency symptoms resolve.

Method of administration:

- FERIFER is for oral use only.
- Can be used between or after meals.
- Daily total dose can be taken in single or divided doses.
- Can be mixed with fruit juices.

Additional information on special populations
Renal/Liver failure:
FERIFER should not be used in serious liver and kidney diseases.

Pediatric population:
FERIFER should be administered pediatric patients as indicated in the posology section.

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

4.3 Contraindications

- Subjects with known hypersensitivity to active substance or any of the excipients
- All types of anemia not caused by iron deficiency (e.g., hemolytic anemia)
- Iron overload (hemochromatosis, chronic hemolysis),
- Hypersensitivity to iron, disturbances in iron utilization (lead anemia, sideroacrestic anemia)
- Thalassemia
- Serious liver or renal diseases
- Regular blood transfusions
- Daily iron supplementation should not be recommended for patients with HIV infection unless iron deficiency anemia is clinically confirmed.

4.4 Special warnings and precautions for use

- Anemia should always be treated under a physician's supervision.
- If treatment is not successful (if hemoglobin levels fail to rise approximately 2-3 gr/dl after 3 weeks), treatment should be revised.
- Patients who receive regular blood transfusions should be warned for iron overload if iron is administrated along with erythrocytes.
- It should be used with caution in case of alcoholism and intestinal inflammation.
- It should be used with caution in patients with gastric ulcers.
- Dark discoloration of stool may occur during treatment with oral iron preparations; this is an expected condition which does not require any measures. This does not cause false results on fecal occult blood tests. Therefore, there is no need to stop treatment during the examination.
- In anemia of infections or malignancies, supplemented iron is stored in the reticuloendothelial system and it is mobilized to become available after the primary disease is cured.
- Should not be taken with milk.
- Accidental ingestion of iron-containing products in children can lead to fatal poisoning. Keep out of reach of children.

- Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrose - isomaltase insufficiency should not use this medicine due to the sucrose it contains.
- It contains (methyl paraben sodium, propyl paraben sodium) that may cause delayed allergic reaction.
- This medicinal product contains 0.003 mmol sodium per 1 ml (20 drops). Contains less than 1 mmol (23 mg) sodium; so it's actually "sodium free".

4.5 Interactions with other medicinal products and other forms of interaction
The interactions that occur when divalent iron preparations are taken with food and certain drugs (tetracyclines etc.) are not expected with trivalent iron-hydroxide polymaltose complex included in the composition of FERIFER. However, due to potential interaction with calcium-containing preparations, they should be used minimum 2 hours apart.

Vitamin C is known to increase iron absorption.

When levothyroxine-containing drugs are taken together with FERİFER, the absorption of the two drugs should be interrupted for at least 2 hours.

4.6 Pregnancy and lactation
General recommendation
Pregnancy category A

• Despite this pregnancy category, the doctor makes the final decision of the pregnant woman whether to use the drug or not; It should be given by making a detailed benefit-risk assessment according to the gestational week, the existing/detected disease of the pregnant woman and other characteristics.
• Although the risk categories help the health personnel about the potential risk of the drug in pregnancy, the evaluation of the doctor is essential.

Women of childbearing potential/Birth control (Contraception)
Used for iron supplementation in pregnancy.

Well-managed epidemiological studies have not demonstrated any adverse effects of Iron III Hydroxide Polymaltose Complex on pregnancy or fetal/newborn infant health.

Pregnancy
FERIFER can be used in pregnancy by consulting a doctor.

Lactation
Iron is secreted into mother milk. The secretion does not vary by the mother’s iron levels or the amount of dietary iron. Therefore, iron supplementation to a breast-feeding mother does not cause iron intoxication or does not eliminate already present iron deficiency in the infant. FERIFER can be used during lactation by consulting a doctor.

Reproduction / Fertility
It has no effects on reproduction.

4.7 Effects on ability to drive and use machines
It has no potential effects on the ability to drive and use machines.

4.8 Undesirable Effects
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 (cannot be estimated by available data)

Immune system disorders
Very rare: Allergic reactions, asthma

Nervous system disorders
Uncommon: Headache

Gastrointestinal disorders
Uncommon: Feeling of fullness, epigastric discomfort, nausea, constipation, diarrhea, abdominal pain, vomiting, reversible discoloration of the teeth

Skin and subcutaneous tissue disorders
Uncommon: Urticaria, rash, exanthema, pruritus.
Very rare: Localized skin reactions

Renal and urinary system disorders
Rare: Urine discoloration
Note: Iron related stool discoloration is common.

Iron III hydroxide polymaltose does not cause undesirable effects such as teeth discoloration or metallic taste in mouth that occur with medicines containing divalent ionized iron salts.

4.9 Overdose
Acute iron intoxication is not common in adults. It is more common in young children. An overdose of more than 20 mg per kilogram body weight poses a potential risk. In young children, a total of 0.5 g iron ingestion may cause life-threatening conditions, while doses exceeding 1-2 g may be fatal.
Four typical phases can be observed in intoxication. Nausea, vomiting, diarrhea occurs in the first 6 hours following ingestion. Hypotension, shock, acidosis, convulsions can be seen at high doses (over 20 mg/kg). In mild cases, an improvement follows in the second phase Potential findings of the third phase (after 12-18 hours) are liver damage, tubular necrosis, cardiovascular shock and coagulopathy. In the fourth phase (within 2-6 weeks) stenosis of the esophagus, stomach and duodenum occurs.

Management:
If a high dose is ingested, gastric lavage is performed-or if not possible-vomiting can be induced. Bowel irrigation can be performed as an advanced measure. If serum iron concentration is 3.5-5 mg/L (63-85 mmol) and severe clinical signs of iron intoxication are present, renal excretion should be stimulated by a chelating agent (Desferrioxamine). Desferrioxamine is administered intravenously at a dosage of 15 mg/kg/hour; maximum dose is 80 mg/kg/24 hours. Other chelating agents such as sodium-EDTA can also be used. Supportive treatment in shock is i.v. perfusion.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Trivalent Iron Preparation, Antianemic drug.
ATC code : B03AB05

Iron is present in every cell of the body and has vital functions. Ionic iron is involved in the structure of enzymes that play a role in energy transfer (cytochrome oxidase, xanthin oxidase, succinic dehydrogenase). Deficiency in such vital functions occurs in case of iron deficiency. As a result of Iron III hydroxide polymaltose complex administration, reduced blood forming and related effects of iron deficiency anemia is resolved by means of iron III ion.

Daily recommended amounts of iron required to enter systemic circulation (RDA):

0-6 months	6 mg
6-12 months	10 mg
1-3 years	10 mg
4-6 years	10 mg
7-10 years	10 mg
Over 11 years	12-15 mg
Pregnant women	30 mg
Breast-feeding mothers	15 mg

FERIFER is developed for treatment and prophylaxis of iron deficiency.
FERIFER does not cause undesirable effects such as teeth discoloration and metallic taste in mouth, seen with bivalent ionized iron salt preparations.

5.2 Pharmacokinetic properties

General Properties

Absorption

FERIFER is rapidly absorbed following oral administration. The amount of iron absorbed depends on degree of the iron deficiency in the treated subject. Absorption increases to the extent of iron deficiency.

Distribution

Absorbed iron is either used for hemoglobin and myoglobulin synthesis or transported to iron stores. As a result, iron deficiency symptoms resolve.

Biotransformation

No relevant information is reported.

Elimination

Iron that is not absorbed from the gastrointestinal tract is excreted in feces.

5.3 Preclinical safety data

Based on conventional safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and reproduction toxicity studies, does not present any specific hazard for humans.

In animal studies on white mice and rats, LD50 value for Iron III Hydroxide Polymaltose Complex could not be identified at oral doses of iron up to 200 mg per kilogram of body weight.

6. PHARMACEUTICAL PROPERTIES

6.1 List of excipients

Sucrose
Methyl paraben (E218)
Propyl paraben (E216)
Cream flavor
Sodium Hydroxide
Purified water

6.2 Incompatibilities

There is no evidence that FERIFER is incompatible 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 an oral drop presented in 30 ml amber colored glass vial (Type III) closed with HDPE cap with LDPE dropper seal in the primary packaging material.

Each carton contains one bottle.

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

Berko İlaç ve Kimya San. A.Ş.
Yenişehir Mah. Özgür Sok. No: 16-18 Ataşehir/İstanbul-Türkiye
+90 216 456 65 70 (Pbx)
+90 216 456 65 79 (Fax)
info@berko.com.tr

8. MARKETING AUTHORIZATION NUMBER(S)

2016/144

9. DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

Date of first authorization: 10.03.2016
Date of latest renewal: 07.02.2021

10. DATE OF REVISION OF THE TEXT

04.05.2020