SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

FERIFER-40 ORAL SOLUTION

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml of solution (1 spoonful) contains;

Active substance(s):

117.65 mg of iron III hydroxide polyimaltose complex equivalent to 40 mg of iron (III)

Excipients:

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

For the 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.

4.2 Posology and method of administration

Posology/frequency of administration and duration of the treatment

FERIFER-40; is used at doses equivalent to elementary iron doses of 40-80 mg in children, 80-120 mg in adults.

If not advised otherwise by the doctor, it is used at the following doses:

- Children: 1-2 times 1 spoon (5 ml) in a day
- Adults: 2-3 times 1 spoon (5 ml) in a day

Duration of the treatment:

Treatment should be continued until the hemoglobin level reaches normal limits (usually 8 to 12 weeks), then at least to fill the iron stores.

Method of administration

FERIFER-40 spoons is taken directly from the oral route.
It can be used with meals or after meals.
It can be mixed with fruit or vegetable juices.

Additional information for special populations
Renal/hepatic failure:
FERIFER-40 should not be used in severe liver and kidney diseases

Pediatric population:
FERIFER-40 should be administered in pediatric patients as indicated in the posology section.

Geriatric population:
Administration in elderly is the same as in adults.

4.3. Contraindications
Subjects with known hypersensitivity to active substance or any of the excipients in the product.
All types of anemia not caused by iron deficiency (e.g. hemolytic anemia)
Iron overload (hemochromatosis, chronic hemolysis)
Hypersensitivity to iron, disturbances in utilization of iron (lead anemia, sidero-achrestic anemia)
Thalassemia
Severe liver and kidney diseases
Regular blood transfusions

In HIV-infected patients, daily iron supplement therapy should not be performed unless anemia due to iron deficiency is clinically confirmed

4.4. Special warnings and precautions for use
Anemia should always be treated under the supervision of a doctor.

If the 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 cases of anemia due to infection or malignancy, supplemented iron is stored in the reticuloendothelial system from which it is mobilized and utilized after treating the primary disease.

It 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 fructose intolerance problems should not use this medicine because it contains sorbitol 70% (E420).

It contains methyl paraben sodium (E219) and propyl paraben sodium (E217), which may cause allergic reactions (possibly delayed).

4.5 Interaction with other medicinal products and other forms of interaction

The interactions that occur when bivalent 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.

When medicines containing levothyroxine are taken simultaneously with FERIFER-40, the absorption is impaired. Therefore, the two medicines should be taken at least 2 hours apart.

Vitamin C is known to increase iron absorption.

Additional information for special populations:
There are no interaction studies.

Pediatric population:
There are no interaction studies.

4.6. Fertility, pregnancy and lactation

General advise:
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, 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 physician is essential.

Women of childbearing capacity / Birth control (Contraception)
There is no specific data on women with childbearing potential and birth control.

Pregnancy
It is used as an iron supplement 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.
FERIFER-40 can be used during pregnancy period after consulting with the physician.

Breast-feeding
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.

Fertility
There is no effect on reproductive ability.

4.7 Effects on ability to drive and use machines
It has no negative effect on ability to drive and use of machines.

4.8 Undesirable effects
Undesirable effects are classified according to the rule mentioned below:
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 (can not be estimated based on available data).

Immune system diseases:
Very rare: Allergic reactions, asthma

Nervous system diseases
Uncommon: Headache

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

Skin and subcutaneous diseases:
Uncommon: Urticeria, skin rash, exanthema, pruritus.
Very rare: Localized skin reactions.

Kidney and urinary system diseases:
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 bivalent ionized iron salts.

Reporting of suspected adverse reaction
Reporting suspected adverse reactions after authorization 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 Turkish Pharmacovigilance Center (TÜFAM). (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; tel.: 0 800 314 00 08; fax: 0 312 218 35 99)

4.9 Overdose and treatment
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 oral iron preparations
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, xanthine oxidase, succinic dehydrogenase). Deficiency in such vital functions occur 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.

5.2 Pharmacokinetic Properties:

General characteristics

Absorption
FERIFER-40 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:
Iron is bound to plasma proteins and hemoglobin at 90% ratio.

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

Biotransformation:
Iron is kept in a dynamic equilibrium in plasma. While a complex of new transferrin-iron is formed by the iron from intestines, majority of iron transferred as bound to transferrin (approximately 80%) is transferred to precursor cells in the bone marrow and hepatic reticuloendothelial cells. Iron-transferrin complex enters the cell via receptor mediated endocytosis and it is taken into a non-lysosomal acidic vesicle. Then iron is detached from the complex and the remaining apotransferrin-receptor complex returns the membrane and it is used there. Iron is adhered to protoporphyrine by transferring into erythroid cells or mitochondria, and it is converted immediately or it is stored after binding with ferritin. Number of receptors is increased in iron deficiency.

Elimination
Iron that is not absorbed from the gastrointestinal tract is excreted in feces.
Only 1 mg iron is eliminated via bile and urinary tract. Additionally, women lose iron during menstruation. Plasma half-life is 1.5 hours.

Linearity/Non-linearity:
Its pharmacokinetics is linear. Plasma levels show increase in accordance with the administered doses.

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 2000 mg per kilogram of body weight.

6. PHARMACEUTICAL PARTICULARS

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

6.2. Incompatibilities
There is no evidence that FERIFER-40 is incompatible with any drug or substance.

6.3. Shelf life
24 months

6.4 Special precautions for storage
Store at the room temperature below 25°C.

6.5 Nature and contents of container

FERIFER is presented as 10 or 28 disposable spoons in 5 ml PET spoons, each of which is covered by aluminum folio. These spoons also packed in PVC separator.

All forms may not be present in the market.

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)
229/88

9. DATE OF FIRST AUTHORIZATION / RENEWAL OF THE AUTHORIZATION
Date of first authorization: 24.02.2011
Date of latest renewal: 14.06.2016

10. DATE OF REVISION OF THE TEXT
10.03.2020