FerroZinc® Syrup, 100 ml

The formula:
Each 5 ml (1 measuring cup) of syrup contains 39.77 mg iron (as ferrous fumarate), 15 mg zinc (as zinc sulphate heptahydrate), 200 mcg folic acid, 50 mg vitamin C as active substances and 1500 mg sorbitol (70%), 5 mg methylparaben sodium, 1 mg sodium saccharin, 750 mg fructose, 125 mg sodium hydroxide, 2.53 mg sodium acetate, 5 mg sodium cyclamate and also citric acid monohydrate, neohesperidin DC 10%, orange flavour, lemon flavour, tangerine flavour, vanilla flavour and deionized water as excipients.

The reservoir cap contains 1000 mg Vitamin C and 4 mg Folic acid to be mixed into the solution at the time of administration.

Pharmacological properties
Pharmacotherapeutic group: Vitamin, mineral combinations
ATC Code: A11JB

Pharmacodynamic properties:
Iron is an essential constituent of the body. It has important functions such as haemoglobin formation in blood, carrying oxygen into the tissues, maintenance of oxidative processes. Ferrous fumarate, a salt including valence 2 ferrous in large amounts, is used in cases when the need for iron is increased e.g. during pregnancy and for the treatment of iron deficiency anaemia. Ferrous (+2 valence) salts are absorbed from the gastrointestinal tract threefold more than iron salts in the ferric (+3 valence) form. Folic acid is one of the absolute necessary vitamins for the body. The body's need for folate is increased especially during pregnancy and breastfeeding. In such cases, in order not to result in deficiency, folic acid supplements should be taken. Ascorbic acid included in FerroZinc Syrup containing haematinic essential factors such as folic acid and ferrous fumarate, increases iron absorption to maximum levels, while also compensates Vitamin C deficiency. Ascorbic acid (Vitamin C) helps assimilation of iron and is also involved in haemoglobin formation. Zinc is a metal found in the structure of various enzymes such as dehydrogenase, aldolase peptidase phosphotase, isomerase, phospholipase, which have important roles in carbohydrate, protein and lipid metabolism. Also, it is present in pyridine nucleotide dependent enzymes in large amounts and serves as a cofactor in many enzyme systems. As a result of zinc deficiency of organism protein and carbohydrate metabolism is impaired, learning capacity diminishes and retarded growth occurs. Zinc has multiple functions such as DNA and RNA, protein synthesis, insulin activation, wound healing, cell division, taste, sperm formation, and immunity.

Pharmacokinetic properties:
Absorption and bioavailability:
Absorption of ferrous fumarate, when orally administered, varies depending on patient’s condition. The absorption is within 3 to 10% in normal individuals while increasing 20 to 30% in those with iron deficiency. The absorption is more favourable on an empty stomach.
The saturation curve for zinc is non-linear. Given its metabolism, zinc is partially absorbed from the gastrointestinal tract when given via oral route. Food such as whole-wheat bread, milk, cheese and coffee decrease the absorption.

**Distribution:**
Iron is 90% bound to plasma proteins and haemoglobin.

2 to 8% of ionic zinc in blood is bound to low molecular weight serum proteins. Its usual plasma concentration is between 0.7 and 1.5 µg/ml. Plasma concentration of a patient orally receiving 50 mg of elemental zinc is reached approximately to 2.5 µg/ml within 2 to 3 hours.

**Biotransformation:**
Iron is kept in plasma with a dynamic balance. While new transferrin-iron complex is formed with the intestinal iron, major fraction of iron (~80%) which is carried as a combination with transferrin in plasma, is transferred to the precursor cells in bone marrow and hepatic reticuloendothelial cells. Iron-transferrin complex enters into cells via receptor-mediated endocytosis, is taken into a non-lysosomal acidic vesicle and disassociated from the iron-complex, the remaining apotransferrin-receptor complex returns to the membrane and is used here. Iron joins to protoporphyrin and is converted to hem after being transferred to erythroid cells or mitochondrias or stored as being combined with ferritin. Number of receptors increases in case of iron deficiency. The plasma half-life of iron is 1.5 hours.

**Elimination:**
There is no physiological elimination system for iron. However, it is excreted in small amounts through the skin, hair, nail, faeces, breast milk, menstruation and urine. The plasma half-life is 1.5 hours.

Excretion of zinc occurs via the faeces. Small amount of it is excreted via urine. Of the 13.2 mg zinc, which is the daily dietary intake of a normal adult, 5.6 mg is excreted via the faeces and 0.1-0.9 mg through the urine. The kidneys normally have no impact on the regulation of serum zinc and shows highly limited elimination capacity. Even though the amount of orally taken zinc is increased, excretion via the urine does not change, however, when zinc is administered intravenously apparent increase in urinary excretion occurs. Biliary excretion of zinc is very limited when compared to the urinary excretion. Zinc loss via the sweat may be observed. It is reported that 2-3 mg of zinc is lost via the sweat in hot climate. The plasma half-life is 3 hours.

**INDICATIONS:**
It is used in all the iron deficiencies which are originated from various causes and iron deficiency anemia, macrocytic dietary anemia, anemia caused by hemorrhages, iron deficiency in pregnancy, nurseling and children, latent iron deficiency, zinc deficiency with iron deficiency.

**CONTRAINDICATIONS:**
It should not be used in those with overloading of iron in the organism or disturbances in iron utilization (hemochromatosis; hemosiderosis, lead anemia, sideroachrestic anemia and thalassemia) and non-iron deficiency related anemia (e.g. megaloblastic anemia due to Vitamin B12 deficiency, Hemolytic anemia) and patients who receive regular blood transfusions.
Daily therapy should not be implemented in patients with HIV infection, providing that iron deficiency related anaemia is clinically confirmed.

**SPECIAL WARNINGS AND PRECAUTIONS FOR USE:**
Since it would not provide benefits when used for anaemia not dependent iron deficiency and may lead to accumulation of iron in the body, necessary clinical and laboratory investigations should be performed prior to initiation of the therapy. Iron preparations leads to darkening of the faeces colour. This should be explained to the patient in advance.

It should be administered to the patients with stomach ulcers under doctor supervision.

FERROZINC contains 5 mg methyl paraben per each 5 ml. Therefore, allergic reactions (possibly delayed) and extraordinary bronchospasm may occur.

This medicinal product contains fructose and sorbitol. Therefore patients with rare hereditary problems of fructose intolerance should not use this medicine.

If you are on a controlled sodium diet, please note that this medicinal product contains 82.3 mg sodium per each 5 ml.

Accidental intake/swallowing of iron-containing products at doses of 60 mg/kg in children under 6 years of age results in fatal intoxications. Therefore keep these medicines out of reach of children. In cases of overdose, immediately contact your doctor or the National Toxicity Information Center (UZEM).

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

**Pregnancy and lactation:**
Pregnancy category: C.

Pregnant and lactating mothers may use this medicinal product under doctor’s control. Use in pregnant women should be determined after the benefit-risk evaluation by the doctor

**Effects on ability to drive and use machines:**
No negative impact on ability to drive and use machines has been reported.

**SIDE EFFECTS/ ADVERSE EFFECTS:**
The adverse reactions reported have been classified as per the following rule:
(very common (≥ 1/10); common (≥ 1/100 to< 1/10); uncommon (≥ 1/1000 to < 1/100); rare (≥ 1/10.000 to < 1/1000); very rare (< 1/10.000), not known (cannot be estimated from available data).

**Immune system disorders:**
Rare: Allergic Reactions
**Gastrointestinal disorders:**
Rare: Fresh blood in the stool
Common: Diarrhoea, nausea, epigastric pain, constipation, vomiting, darkening of faeces colour.

**Renal and urinary disorder:**
Uncommon: darkening of urine colour.

The reason for such symptoms is irritation which may be prevented by decreasing the dose or taking the medicine after meals. It should be noted that food delays the absorption of iron.

**CONSULT YOUR DOCTOR IN CASE OF AN UNEXPECTED EFFECT.**

**DRUG INTERACTIONS AND THE OTHER INTERACTIONS:**
When taken in combination with antacids such as magnesium trisilicate and carbonate, the treatment may be non-responsive.

Milk and eggs may decrease the absorption of iron.

It should not be administered with tetracycline, cholestyramine, antacids, penicillamine and oral gold compounds. If these must be taken, then administration with several hours intervals must be implemented.

Concomitant uses with salicylates, phenylbutazone and oxyphenbutazone may cause irritation of intestinal mucosa.

Positive results may be obtained by means of the benzidine test during the iron therapy.

Cytostatics, sulphonamides, antiepileptics and barbiturates may decrease the absorption of folic acid.

It should not be taken with penicillin derivatives due to the zinc salt content.

Zinc sulphate constitutes a chelate with tetracyclines, therefore these medicines should not be used concomitantly.

It should not be used with tea, coffee and milk.

It should be used carefully in those with intestinal tumours.

After haemoglobin values are reached to the normal levels, oral iron therapy must be continued until body iron stores are replenished confirmed by monitoring the serum ferritin levels.

**METHOD OF ADMINISTRATION:**
In cases when the need for iron and folic acid is increased e.g. during pregnancy and lactation, and mild iron deficiency anaemia, take 5 ml two times a day using a dose pipette. In cases of anaemia due to severe iron deficiency where haemoglobin levels are decreased to levels below 8-9% gr, take
5 ml four times a day using a dose pipette. To return the iron stores of the organism to the normal levels, treatment should be maintained until the haemoglobin levels are back to the normal. Thereafter, take 5 ml two times a day for 1-3 month. One measuring cup (5 ml) once or twice a day is used for children.

**Preparation of the syrup prior to use:**

1. Pull out the protective seal at the mouth of the bottle by pulling it up in the direction of the arrow. Remove the seal.
2. Press down the plunger and allow the powder load into the bottle.
3. Shake the bottle hardly for 1-2 minutes.
4. Remove the reservoir cap system on the mouth of the bottle while using. Use the appropriate doses of the syrup by pipette and then recap.

Expiration of the resulting syrup is 20 days.

**OVERDOSE AND TREATMENT:**

Long term use and overdose are resulted in hemosiderosis. Liver cirrhosis, pancreatic fibrosis may develop due to accumulation of iron. In case of overdose, an antiemetic must be administered, followed by gastric lavage with 2 g/L desferrioxamine solution. Following the gastric lavage, a solution containing 5 g of desferrioxamine in 50 to 100 ml of water must be introduced into the stomach. Intestinal purge must be achieved by making the patient drink a solution containing mannitol or sorbitol. When the serum iron levels exceeds 142 micromol/L in the presence of shock and/or coma, 5 mg/kg/h desferrioxamine by IV infusion must be instituted, but daily administration of desferrioxamine should not be exceeded 80 mg/kg. In cases of less severe poisoning, desferrioxamine 50 mg/kg IM must be given, however the administered dose should not exceed 4 g. No cases of chronic zinc poisoning have been detected in people. Long term use or administration of high doses may cause copper deficiency and anemia. In this case, in order to make up for copper depletion, copper intake at the dose of 4 mg a day and slow blood transfusion for anemia may be required. In case of zinc poisoning, gastric lavage is implemented and electrolyte balance is achieved.

**SPECIAL PRECAUTIONS FOR STORAGE:**

Prior to be ready for use, store in room temperature under 25°C.

The reconstituted syrup should be stored at room temperature under 25°C and used within 20 days.

Keep out of sight and reach of children and in its packaging.
NATURE AND CONTENTS OF CONTAINER:
Each box contains amber colored glass (Type III) bottle with HDPE protective seal and PP reservoir cap and a 5 ml dose-adjusted pipette.

PRESCRIPTION DRUG

MARKETING AUTHORIZATION HOLDER:
Berko İlaç ve Kimya San. A.Ş.
Address: Yenişehir Mah. Özgür Sok. No: 16-18 Ataşehir/İstanbul
Phone: 0216 456 65 70
Fax: 0216 456 65 79
e-mail: info@berko.com.tr

MARKETING AUTHORIZATION NUMBER(S):

MANUFACTURING SITE:
Berko İlaç ve Kimya San. A.Ş.
Address: Adil Mah. Yörükluer Sok. No: 2 Sultanbeyli/ İstanbul/ TURKEY
Telephone: 00 90 216 592 33 00
Fax: 00 90 216 592 00 62