SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product

Iron III hydroxide polymaltose complex/folic acid 100 mg/0.5 mg capsules
Orofer

2. Qualitative and quantitative composition

Each tablet contains 100 mg of iron III hydroxide polymaltose complex and 0.55 mg of folic acid.

Excipient with known effect
Each tablet also contains 69.75 mg of lactose monohydrate. See section 4.4.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Capsule.

Gelatin capsules size "2" scarlet red body/scarlet red cap imprinted "Orofer" on it containing dark brown powder.

4. Clinical particulars

4.1 Therapeutic indications

Iron III hydroxide polymaltose complex/folic acid is indicated

- for the treatment of iron deficiency anaemia during pregnancy, lactation, anaemia due to post-partum haemorrhage, in infants, adolescents, and adults.
- for the prevention of iron and folic acid deficiency.

4.2 Posology and method of administration

Posology
The recommended normal dose for iron III hydroxide polymaltose complex/folic acid is 1 tablet a day. If deemed appropriate by the physician, 1 tablet may be taken two times a day.

The duration of treatment is determined by a physician.
After the clinical elimination of the symptoms of iron deficiency, the use of iron III hydroxide polymaltose complex/folic acid must be continued for at least an additional month (for replenishment of iron stores).

Special Population

- Geriatric population: normal doses may be used, there is no need for dose adjustment.
- Renal/Hepatic failure: iron III hydroxide polymaltose complex/folic acids must not be used in case of severe liver and kidney diseases.

Paediatric Population
In a pediatric population, syrup may be used.

Method of administration
For oral use.

Iron III hydroxide polymaltose complex/folic acid must be taken with or after meals.

4.3 Contraindications

Iron III hydroxide polymaltose complex/folic acid is contraindicated in patients with
- hypersensitivity to iron, folic acid or any of the excipients ingredients, listed in section 6.1,
- conditions leading to an iron overloading (hemochromatosis, hypersiderosis, chronic hemolysis),
- anaemia not caused by an iron deficiency (such as hemolytic anaemia or megaloblastic anaemia due to vitamin B12 deficiency),
- thalassemia,
- severe liver or kidney diseases,
- conditions, requiring regular and continuous blood transfusions,
- HIV infection without clinically proven iron deficiency anaemia.

4.4 Special warnings and precautions for use

As with other alpha$_1$ blockers, a reduction in blood pressure can occur in individual cases during treatment with tamsulosin prolonged-release tablets, as a result of which, rarely, syncope can occur. At the first signs of orthostatic hypotension (dizziness, weakness), the patient should sit or lie down until the symptoms have disappeared.

General information
- Anaemia must always be treated under supervision by a physician.
- In iron deficiency anaemia, with oral iron treatment, the haemoglobin level is increased by 1-2 g/dl in 2-4 weeks. Therefore, a blood count is requested 2-4 weeks after the initiation of treatment.
- Patients, receiving repeated blood transfusions must be warned against iron overload since each unit of whole blood contains approximately 250 milligrams of iron.
- Caution is necessary in patients with alcoholism and intestinal inflammation.
- Caution is necessary in patients with gastric ulcers.
- During the administration of oral iron formulations, the colour of the stool may darken; this is normal and does not require any measures. I will not cause false positive results during tests for occult blood in stool. Therefore, there is no need to discontinue the treatment during this test.
- In anaemia, associated with infection or malignancy, administered iron is stored in the reticuloendothelial system and is used with mobilization following the treatment of the primary disease.
- The tablet contains folic acid which can mask a deficiency in vitamin B12. Given the risk of irreversible neurological disorders, any possible deficiency in vitamin B12 in an anaemic patient should be excluded before the start of the treatment (see section 4.3).

Pediatric population
Accidental administration of iron-containing products can cause fatal toxicity in children below 6 years of age. In case of overdose, the patients must promptly consult a physician or poison control centre.

Excipients
This medicine contains **lactose**. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Since the iron III ion in iron III hydroxide polymaltose complex is a complex ion, any ionic interaction with food or concomitant drugs (tetracyclines, antacids) is not expected. However, due to the possibility of an interaction with formulations containing calcium, at least 2 hours must be left between the administration of calcium and iron.

4.6 Fertility, pregnancy and lactation

Pregnancy
Pregnancy category: A
This medicine is used as an iron and folic acid supplement in pregnancy. Well-controlled epidemiological studies have shown that iron III hydroxide polymaltose complex has no adverse effects on the health of foetus/newborn or pregnancy, so, iron III hydroxide polymaltose complex/folic acid may be used during pregnancy.

Lactation
This medicine is used as an iron and folic acid supplement during the lactation period.

Iron is excreted into breast milk. This excretion does not change according to the existing iron level of the mother and the quantity of iron taken with food. Therefore, the administration of iron formulations to a lactating mother does not yield an iron intoxication in the baby or the removal of existing iron deficiency in the baby.

Iron III hydroxide polymaltose complex/folic acid may be used during lactation.

Fertility
No effects of iron III hydroxide polymaltose complex/folic acid on fertility have been determined.

4.7 Effects on the ability to drive and use machines
Iron III hydroxide polymaltose complex/folic acid has no effects on the ability to drive vehicles or operate machinery.

4.8 Undesirable effects
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); unknown (unpredictable with the available data).

	Uncommon (≥ 1/1000 to < 1/100)	**Rare (≥ 1/10.000 to < 1/1000)**	**Very rare (< 1/10.000);**
Immune System Disorders			Allergic reactions, Asthma.
Nervous system disorders	Headache.		
Gastrointestinal diseases	Feeling of fullness, Feeling of epigastric heaviness, Nausea, Constipation, Diarrhea, Abdominal pain, Vomiting.		
Skin and subcutaneous disorders	Urticaria, Rashes, Exanthema, Itching.		Localized skin reactions.
Renal and urine tract diseases		Change in urine colour (note: Discoloration of stool may be frequently seen in connection with iron).	

Iron III hydroxide polymaltose does not cause tooth colouring and a metallic taste in the mouth seen with bivalent ionized iron salt preparations.

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 the e-PV desktop applications (https://drive.google.com/file/d/16hwTz0587ZWtSWadbBAMwQPOD_KSExZP/view) or search for e-PV Mobile applications on the Google Play or Apple App Store.

4.9 Overdose

In case of overdose, epigastric pain, diarrhoea and vomiting may be seen and in more severe cases metabolic acidosis, convulsions and coma.

It has been reported that an excessive dose of folic acid could cause changes in the central nervous system (i.e., problems, changes in the rhythm of sleep, irritability, and hyperactivity), nausea, tension abdominal and flatulence.

In case of overdose, the use of desferrioxamine (initially 1000 mg then 500 mg every 4 hours up to two doses IV), or calcium disodium EDTA (167 mg/m2 every 4 hours IM, in the form 1 mg/m2 IV in the form of 8-24 hour infusion or every 12 hours), are recommended *(desferrioxamine has teratogenic effects).*

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacological classification: 10.1.4 Medicines affecting the blood: Combinations.

Orofer contains 100 mg of iron included as iron hydroxide polymaltose complex and 0.550 mg folic acid. This combination has been developed for the prevention and treatment of iron and folic acid deficiencies.

Iron is found in all cells in the body and has vital functions. It is present in the structure of enzymes (cytochrome oxidase, xanthine oxidase, succinic dehydrogenase), which play a role in energy transfer. In the case of iron deficiency, the deficiency of these vital functions is seen. With the application of iron during pregnancy and lactation, the increasing iron requirement of the mother and infant are met and in case there is a deficiency, it is treated.

Folic Acid (Vitamin B9) is transformed to tetrahydrofolate *in vivo* and plays a role in various metabolic processes, including the synthesis of purine and pyrimidine nucleotides and related DNA copying and synthesis, producing new cells, and supporting nerve and immune system. Deficiencies in folic acid can be a serious problem leading to different health problems (poor immune function, chronic low energy, poor digestion, developmental problems during pregnancy and infancy, anaemia, sores in the mouth, and mood changes).

Recommended Daily Allowance Quantities (RDA)

1 µg folate is equivalent to 0.6 µg folic acid.

Age group	**Iron (mg)**	**Folate (µg/day)**
children		
0-6 months	6	65
7-12 months	10	80

1-3 years	10	150
4-6 years	10	200
7-10 years	10	200-300
Women		
11-14 years	15	300
15-18 years	15	400
19-50 years	15	400
> 51 years	10	400
Pregnant women	30	600
Lactating women	15	500
Men		
11-14 years	12	300
15-18 years	12	400
19-50 years	10	400
> 51 years	10	400

Maximum daily allowable total amount

1 µg folate is equivalent to 0.6 µg folic acid.

Age group	***Folate (µg/day)***
children	
0-6 months	UD
7-12 months	UD
1-3 years	300
4-6 years	400

7-10 years	400-600
Men & women	
11-14 years	600
15-18 years	800
19-50 years	1000
> 51 years	1000
Pregnant women	
≤ 18 years	
19-50 years	
Lactating women	
≤ 18 years	
19-50 years	

5.2 Pharmacokinetic properties

Iron

General characteristics

In the Iron hydroxide polymaltose complex, iron III hydroxide cores are surrounded by polymaltose molecules which are bonded superficially with non-covalent bonds. Therefore, in a physiological environment ionic iron is not released and its effective absorption is provided.

Absorption

Iron is absorbed from the intestines on the duodenum and proximal jejunum. The absorption of the iron from intestines varies from person to person and iron deficiency. The daily iron requirement of a normal adult is 0.5 to 1 mg. This value may increase to 1 to 2 mg per day in women during menstruation.

Distribution

70 % of total iron in the body is stored in red blood cells in the form of haemoglobin, 10-20 % is stored in the form of ferritin and hemosiderin, and 10 % in myoglobin. Less than 1 % is found in trace quantities in cytochromes and other enzymes containing iron.

Elimination
Non-absorbed part of iron is excreted in faeces.

Folic acid
General characteristics
Folic acid is a member of the B group of vitamins. Folic acid is reduced to tetrahydrofolate *in vivo*. Tetrahydrofolate is the coenzyme of various metabolic processes, including purine and pyrimidine nucleotides and therefore, DNA synthesis; it has a role in some amino-acid transformations, format formation and use. Deficiency results in megaloblastic anaemia.

Absorption
Folic acid is rapidly absorbed from the gastrointestinal tract, mainly from the duodenum and jejunum and is transferred to portal circulation in unchanged form.

Distribution
In plasma and liver, it is transformed to metabolically active form 5-methyltetrahydrofolate. Folate metabolites undergo enterohepatic circulation. Folate is excreted into breast milk.

Elimination
Surplus folate metabolites are excreted in urine without change.

5.3 Preclinical safety data
Non-clinical data reveal no special hazard for humans based on conventional studies on safety pharmacology, repeated dose toxicity, genotoxicity and toxicity to reproduction.

6. Pharmaceutical particulars

6.1 List of excipients
Lactose monohydrate
Sodium lauryl sulphate
Magnesium stearate
EHG capsule

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Store below 30°C.

6.5 Nature and contents of the container
The capsules are packed in PVC/PVDC/Alu blisters.

Pack sizes: 2 x 20 capsules.

6.6 Special precautions for disposal and handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT

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8. MANUFACTURERS

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9. REGISTRATION DETAILS

Zimbabwe registration number: 2023/10.1.4/6455
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10. DATE OF REVISION OF TEXT

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