# SUMMARY OF PRODUCT CHARACTERISTICS

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## 1. NAME OF THE MEDICINAL PRODUCT

Orofer Syrup

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains:

Iron (III) Hydroxide Polymaltose Complex equivalent to elemental iron……..50 mg

In a flavoured syrup base

## 3. PHARMACEUTICAL FORM

Syrup

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

- For the treatment of iron deficiency anemia
- For the treatment of iron deficiency anemia during pregnancy, lactation, anemia due to postpartum hemorrhage, infancy, adolescents and adults.

### 4.2 Posology and method of administration

Adults: 5 ml to be taken 2-3 times daily

Children: 5 ml to be taken 1-2 times daily

Infants: begin with 2.5 ml once or twice daily. Depending on the clinical improvement of the patient, increase the dose to 5 ml once or twice daily.

Or as directed by physician.

Orofer syrup may be mixed with fruit or vegetable juices or other liquids if desired.

### 4.3 Contraindications

Iron (III) hydroxide polymaltose complex is contraindicated in iron overload, thalassaemia and anemia not caused by iron deficiency and known hypersensitivity to iron polymaltose or to any of the excipients.

**4.4 Special warnings and precautions for use**

Caution is advised in patients who may have folate dependant tumors.

No special precaution is required.

In cases of anemia due to infection or malignancy, the substituted iron stores in the reticulo-endothelium system from which it is mobilized and utilized only after correcting the primary disease.

Regular monitoring of the haematologic response is required during Orofer therapy as a risk of iron overload and liver damage exists if too much Orofer is ingested by haemachromatosis patients over a long period of time.

Laboratory tests: Regular monitoring of Hb levels and serum ferritin levels should be performed to assess the response to supplementation with Orofer as deemed appropriate by the medical practitioner.

**4.5 Interaction with other medicinal products and other forms of Interaction**

Iron absorption from iron polymaltose complex was not reduced by aluminium hydroxide or tetracycline. Iron (III) hydroxide polymaltose complex can therefore be administered at the same time as tetracycline or other phenolic compounds, as well as aluminium hydroxide.

Animal studies with tetracycline, aluminium hydroxide, acetylsalicylate, sulphasalazine, calcium carbonate, calcium acetate and calcium phosphate in combination with vitamin D3, bromazepam, magnesium aspartate, D-penicillamine, methyldopa, paracetamol and auranofin have not shown any interactions with iron polymaltose complex.

Concomitant administration of parenteral iron and Orofer is not recommended since the absorption of oral iron would be inhibited.

**4.6 Pregnancy and Lactation**

Iron polymaltose complex have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus after the first trimester. Studies in animals have not shown any direct or indirect toxicity affecting pregnancy, embryo development or foetal development.

Human breast milk naturally contains iron, which is bound to lactoferrin. The amount of iron passing from iron polymaltose to the mother's milk is unknown. However, during pregnancy and lactation, this medicine should be used only if the potential benefit outweighs the risk.

**4.7 Effects on ability to drive and use machines**

None

**4.8 Undesirable Effects**

The safety and tolerability of iron polymaltose complex has been evaluated in numerous clinical trials and published reports.

The following adverse reactions have been observed and reported with the following frequencies: Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from the available data).

| System organ class | Frequency | Adverse reactions |
|---|---|---|
| **Gastrointestinal disorders** | Very common | Discolored feces |
| | Common | Diarrhea, nausea, dyspepsia |
| | Uncommon | Vomiting, constipation, abdominal pain, tooth discoloration |
| **Skin and subcutaneous tissue disorders** | Uncommon | Rash, pruritus |
| **Nervous system disorders** | Uncommon | Headache |

**4.9 Overdose**

In cases of overdose, neither intoxication nor iron overload have been reported up to date, due to the low toxicity of iron polymaltose complex.

Keep this product out of the reach of children.

Overdose of iron may cause haemosiderosis and consequent cirrhosis of the liver, diabetes and heart failure. Periodic monitoring of serum ferritin may be useful in recognizing a deleterious, progressive accumulation of iron.

In case of accidental overdose, call a doctor or poison control centre immediately or should be treated with supportive measures and, if required, an iron chelating agent.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties:

**Pharmacotherapeutic Group:** Iron preparations.

**ATC Code:** B03AB05

In iron (III)-hydroxide polymaltose complex, the polynuclear iron (III)-hydroxide core is superficially surrounded by a number of non-covalently bound polymaltose molecules resulting in an overall average molecular weight of approximately 50 kDa. The polynuclear core of IPC has a structure similar to that of the physiological iron storage protein, ferritin. IPC is a stable complex and does not release large amounts of iron under physiological conditions. Because of its size, the extent of diffusion of IPC through the membrane of the mucosa is about 40 times less than that of the hexaquo-iron (II) complex. Iron from IPC is taken up in the gut via an active mechanism. In contrast to iron (II) salts, IPC does not have pro oxidative properties.

### 5.2 Pharmacokinetic properties:

Studies using the twin-isotope technique ($^{55}Fe$ and $^{59}Fe$) have shown that absorption of iron measured as haemoglobin in erythrocytes is inversely proportional to the dose given (the higher the dose, the lower the absorption). There is a statistically negative correlation between the extent of iron deficiency and the amount of iron absorbed (the higher the iron deficiency, the better the absorption). The highest absorption of iron is in the duodenum and jejunum. Iron which is not absorbed is excreted via the faeces. Excretion via the exfoliation of the epithelial cells of the gastro-intestinal tract and the skin as well as perspiration, bile and urine only amount to approximately 1mg of iron per day. For women, iron loss due to menstruation has also to be taken into account.

### 5.3 Preclinical safety data

No $LD_{50}$ for iron polymaltose could be determined in animal studies with white mice and rats up to an orally administered dose of 2,000mg of iron per kilogram body weight.

Effects on fertility: Fertility studies of iron polymaltose in animals did not reveal any effects on fertility or early embryonic development.

No effects of iron polymaltose on development or growth of off spring were observed in a pre/post-natal toxicity study in rats, in which nursing dams were treated throughout the pre-weaning lactation period. Preliminary data from studies conducted in juvenile rats showed no treatment-related adverse effect when immature rats were directly treated orally with iron polymaltose from shortly after birth up to sexual maturity.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipient(s)

Sucrose
Sorbitol 70%
Methyl Paraben
Propyl Paraben
Creamy milk TP essence
Purified water
Sodium Hydroxide

### 6.2 Incompatibilities

No interactions of Iron Polymaltose Complex are evident either with food or medications.

### 6.3 Shelf-life

36 months.

### 6.4 Special precautions for storage

Store in a cool place, below 25$^{o}$C.

**6.5 Nature and contents of container**

150 ml syrup is filled in a amber coloured PET bottle and bottle is sealed with a cap. One measuring cap is placed on the bottle. Each bottle is placed in a printed carton along with leaflet.

**6.6 Instructions for use and handling**

Store in a cool place, below 25$^{o}$C.
Keep away from the reach of children.

**7. MARKETING AUTHORISATION HOLDER**

Emcure Pharmaceuticals Limited

**8. MARKETING AUTHORISATION NUMBER(S)**

Shall be provided when available.

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Shall be provided when available.

**10. DATE OF REVISION OF THE TEXT**

12.03.2020