MonoFer®

# SUMMARY OF

# PRODUCT CHARACTERISTICS

PHARMACOSMOS

MonoFer®

## SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

## 1. NAME OF THE MEDICINAL PRODUCT

Monofer 100 mg/ml solution for injection/infusion

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One millilitre of solution contains 100 mg iron as iron(III) isomaltoside 1000

1 ml vial/ampoule contains 100 mg iron as iron(III) isomaltoside 1000
2 ml vial/ampoule contains 200 mg iron as iron(III) isomaltoside 1000
5 ml vial/ampoule contains 500 mg iron as iron(III) isomaltoside 1000
10 ml vial/ampoule contains 1,000 mg iron as iron(III) isomaltoside 1000

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Solution for injection/infusion.
Dark brown, non-transparent solution.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Monofer is indicated for the treatment of iron deficiency anaemia in the following conditions:
- When oral iron preparations are ineffective or cannot be used
- Where there is a clinical need to deliver iron rapidly

The diagnosis of iron deficiency anaemia should be based on appropriate laboratory tests (e.g. serum ferritin, serum iron, transferrin saturation or hypochromic red cells).

### 4.2 Posology and method of administration

**Calculation of the cumulative iron dose:**

*Iron replacement in patients with iron deficiency anaemia:*
The dose and dosage schedule for Monofer must be individually established for each patient. The optimal haemoglobin target level and iron stores may vary in different patient groups and between patients. Please refer to official guidelines. The dose of Monofer is expressed in mg of elemental iron.

Iron deficiency anaemia will not appear until essentially all iron stores have been depleted. Iron therapy should therefore replenish both haemoglobin iron and iron stores.

After the current iron deficit has been corrected, patients may require continued therapy with Monofer to maintain target levels of haemoglobin and acceptable limits of other iron parameters.

The cumulative iron dose can be determined using either the Ganzoni formula (1) or the dosing table below (2). It is recommended to use the Ganzoni formula in patients who are likely to require individually adjusted dosing such as patients with anorexia nervosa, cachexia, obesity, pregnancy or anaemia due to bleeding.

Haemoglobin is abbreviated Hb.

1. Ganzoni formula:

| Iron dose | = | Body weight(A) | x | (Target Hb – Actual Hb)(B) | x | 2,4(C) | + | Iron for iron stores(D) |
|---|---|---|---|---|---|---|---|---|
| [mg iron] | | [kg] | | [g/dl] | | | | [mg iron] |

(A) It is recommended to use the patient's ideal body weight or pre-pregnancy weight
(B) To convert Hb [mM] to Hb [g/dl] you should multiply Hb [mM] by factor 1.61145
(C) Factor 2.4 = 0.0034 x 0.07 x 10,000
0.0034: Iron content of haemoglobin is 0.34%
0.07: Blood volume 70 ml/kg of body weight ≈ 7% of body weight
10,000: The conversion factor 1 g/dl = 10,000 mg/l
(D) For a person with a body weight above 35 kg, the iron stores are 500 mg or above

**4.3 Contraindications**

- Hypersensitivity to the active substance, to Monofer or any of its excipients listed in section 6.1
- Known serious hypersensitivity to other parenteral iron products
- Non-iron deficiency anaemia (e.g. haemolytic anaemia)
- Iron overload or disturbances in utilisation of iron (e.g. haemochromatosis, haemosiderosis)
- Decompensated liver cirrhosis and hepatitis

**4.4 Special warnings and precautions for use**

Parenterally administered iron preparations can cause hypersensitivity reactions including serious and potentially fatal anaphylactic/anaphylactoid reactions. Hypersensitivity reactions have also been reported after previously uneventful doses of parenteral iron complexes.

The risk is enhanced for patients with known allergies including drug allergies, including patients with a history of severe asthma, eczema or other atopic allergy.
There is also an increased risk of hypersensitivity reactions to parenteral iron complexes in patients with immune or inflammatory conditions (e.g. systemic lupus erythematosus, rheumatoid arthritis).

Monofer should only be administered when staff trained to evaluate and manage anaphylactic reactions is immediately available, in an environment where full resuscitation facilities can be assured. Each patient should be observed for adverse effects for at least 30 minutes following each Monofer injection. If hypersensitivity reactions or signs of intolerance occur during administration, the treatment must be stopped immediately. Facilities for cardio respiratory resuscitation and equipment for handling acute anaphylactic/anaphylactoid reactions should be available, including an injectable 1:1000 adrenaline solution. Additional treatment with antihistamines and/or corticosteroids should be given as appropriate.

Parenteral iron should be used with caution in case of acute or chronic infection.

Monofer should not be used in patients with ongoing bacteraemia.

Hypotensive episodes may occur if intravenous injection is administered too rapidly.

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

As with all parenteral iron preparations the absorption of oral iron is reduced when administered concomitantly. Oral iron therapy should not be started earlier than 5 days after the last injection of Monofer.

Large doses of parenteral iron (5 ml or more) have been reported to give a brown colour to serum from a blood sample drawn four hours after administration.

Parenteral iron may cause falsely elevated values of serum bilirubin and falsely decreased values of serum calcium.

**4.6 Fertility, pregnancy and lactation**

There are no adequate and well-controlled trials of Monofer in pregnant women. A careful risk/benefit evaluation is therefore required before use during pregnancy and Monofer should not be used during pregnancy unless clearly necessary (see section 4.4).

Iron deficiency anaemia occurring in the first trimester of pregnancy can in many cases be treated with oral iron. Treatment with Monofer should be confined to second and third trimester if the benefit is judged to outweigh the potential risk for both the mother and the foetus.

There is no information available on the excretion of Monofer in the human breast milk.

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

No studies on the effects on the ability to drive and use machines have been performed..

**4.8 Undesirable effects**

Due to limited clinical data on Monofer the mentioned undesirable effects are primarily based on safety data for other parenteral iron solutions.

### 4.9 Overdose

The iron(III) isomaltoside 1000 in Monofer has a low toxicity. The preparation is well tolerated and has a minimal risk of accidental overdosing.

Overdose may lead to accumulation of iron in storage sites eventually leading to haemosiderosis. Monitoring of iron parameters such as serum ferritin may assist in recognising iron accumulation. Supportive measures such as chelating agents can be used

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Iron parenteral preparation, ATC code: B03AC

Monofer solution for injection is a colloid with strongly bound iron in spheroidal iron-carbohydrate particles. Each particle consists of an iron(III) core and a carbohydrate shell of isomaltosides that surrounds and stabilises the core. The chelation of iron(III) with a carbohydrate shell confers to the particles a structure resembling ferritin that is suggested to protect against the toxicity of unbound inorganic iron(III).

The iron is available in a non-ionic water-soluble form in an aqueous solution with pH between 5.0 and 7.0. The toxicity is low and Monofer can therefore be administered in large doses.

Evidence of a therapeutic response can be seen within a few days of administration of Monofer as an increase in the reticulocyte count.

Serum ferritin peaks approximately 7 to 9 days after an intravenous dose of Monofer and slowly returns to base-line after about 3 weeks.

### 5.2 Pharmacokinetic properties

The Monofer formulation contains iron in a strongly bound complex that enables a controlled and slow release of bioavailable iron to iron-binding proteins with little risk of free iron.

Following intravenous administration, iron isomaltoside 1000 is rapidly taken up by the cells in the reticuloendothelial system (RES), particularly in the liver and spleen from where iron is slowly released. The plasma half-life is 5 hours for circulating iron and 20 hours for total iron (bound and circulating).

Circulating iron is removed from the plasma by cells of the reticuloendothelial system which split the complex into its components of iron and isomaltoside 1000. The iron is immediately bound to the available protein moieties to form hemosiderin or ferritin, the physiological storage forms of iron, or to a lesser extent, to the transport molecule transferrin. This iron, which is subject to physiological control, replenishes haemoglobin and depleted iron stores.

Iron is not easily eliminated from the body and accumulation can be toxic. Due to the size of the complex, Monofer is not eliminated via the kidneys. Small quantities of iron are eliminated in urine and faeces.

Isomaltoside 1000 is either metabolised or excreted.

### 5.3 Preclinical safety data

Iron complexes have been reported to be teratogenic and embryocidal in non-anaemic pregnant animals at high single doses above 125 mg iron/kg body weight. The highest recommended dose in clinical use is 20 mg iron/kg body weight.

There are no other additional preclinical data of relevance to the prescriber than those already included in other sections of the SPC.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Water for injections
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)

### 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6

**PHARMACOSMOS**

Pharmacosmos A/S
Rørvangsvej 30
4300 Holbæk
www.pharmacosmos.com
www.monofer.com