Product	Venofer Ampoules	
Country	Indonesia	
Manufacturer	SGD	
SAP Number	VNF_LFT_01S_ AMP_ID	**Min. Ver.:** 04
Manufacturer Identification Number	XXXXX/XX/XX	
Fonts	Univers (min. 9 pt)	
Dimensions	148 x 420 mm	

Colours/Flats
Black

Non-Printed Colours
Dye Cut

Venofer®

combiphar

Iron sucrose complex

Injection

Composition
Each 5 mL ampoule contains 20 mg/mL Iron as Iron Sucrose corresponding to 100 mg Iron per ampoule.

List of excipients
Excipients:
Water for injection
Sodium hydroxide (for pH adjustment)

Product description
Venofer is supplied as a dark brown, non transparent, aqueous, solution with a pH of 10.5-11.0 and an osmolarity of 1,150-1,350 mOsmol/l.

Mode of action
Pharmacological Properties
Pharmacodynamic Properties
The ferrokinetics of Venofer labelled with ^{59}Fe and ^{52}Fe were assessed in 5 patients with anaemia and chronic renal failure. Plasma clearance of ^{52}Fe was in the range of 60 to 100 minutes. ^{52}Fe was distributed to the liver, spleen and bone marrow. At two weeks after administration, the maximum red blood cell utilisation of ^{59}Fe ranged from 62% to 97%.

Pharmacokinetic Properties
Following intravenous injection of a single dose of Venofer containing 100 mg Fe (III) in healthy volunteers, maximum iron levels, averaging 538 µmol/L, were obtained 10 minutes after injection. The volume of distribution of the central compartment corresponded well to the volume plasma (approx. 3 Litres).
The iron injected was rapidly cleared from the plasma, the terminal half-life being approx. 6 h. The volume of distribution at steady state was about 8 Litres, indicating a low iron distribution in the body fluid. Due to the lower stability of iron sucrose in comparison to transferrin, a competitive exchange of iron to transferrin was observed. This resulted in iron transport of approx. 31 mg Fe (III) / 24 h.
Renal elimination of iron, occurring in the first 4 h after injection, corresponds to less than 5% of the total body clearance. After 24 h the plasma levels of iron were reduced to the pre-dose iron level and about 75% of the dosage of sucrose was excreted.

Preclinical Safety Data
There are no preclinical data of relevance to the prescriber that are additional to information already in other sections of the SPC.

Indications
Adult
Venofer is indicated for the treatment of iron deficiency in adult patients in the following indications:
- Where there is a clinical need for a rapid iron supply,
- In patients who cannot tolerate oral iron therapy or who are non-compliant,
- Where oral iron preparations are ineffective

Venofer should only be administered where the indication is confirmed by appropriate investigations (in adult patients with Haemoglobin 7 – ≤13 g/dL and hematocrit <39% (man) or Hb 7 – <12 g/dL and hematocrit <36% (Non-pregnant women) and serum ferritin <15 µg/L (man or women with depleted iron stores or adult patients who have CKD with TSAT <25%).

Pediatric
Venofer is indicated for iron maintenance treatment in Pediatric Patients (2 years of age and older) with Haemodialysis Dependent-Chronic Kidney Disease.

Contraindications
The use of Venofer is contraindicated in cases of:
- known hypersensitivity to Venofer of any of its excipients
- anaemias not attributable to iron deficiency
- iron overload or disturbances in utilization of iron
- patients with a history of asthma, eczema or other atopic allergy, because they are more susceptible to experience allergic reactions
- pregnancy first trimester
- history of cirrhosis or hepatitis or the presence of serum transaminase at three times the upper limit
- acute or chronic infection, because parenteral iron administration may exacerbate a bacterial or viral infection

Undesirable Effects
Very rarely anaphylactic like reactions may occur. These may be potentially fatal.
Occasionally the following undesirable effects have been reported with a frequency ≥ one percent: metallic taste, headache, nausea, vomiting, hypotension, hypertension, and injection/infusion site reaction.
Less frequently paraesthesia, abdominal disorders, muscular pain, fever, urticaria, flushing, oedema of the extremities, dyspnoea, anaphylactoid (pseudoallergic) reactions, dizziness, pruritus, rash, asthenia, fatigue, syncope, somnolence, palpitations, chromaturia, chest pain, hyperdrosis, and pyrexia have been reported. In the region of the punctured vein, phlebitis and venous spasm have been observed.
Undesirable effects under investigations including alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, serum ferritin increased, and blood lactate dehydrogenase increased.

Special Warnings and Precautions for Use
Parenterally administered iron preparations can cause severe allergic or anaphylactoid reactions. Which may be potentially fatal. Therefore, facilities for cardio-pulmonary resuscitation must be available.

In the event of a serious anaphylactic or allergic reaction, administration of Venofer must be stopped, intramuscular adrenaline should be administered immediately and other supportive measures initiated in line with the established cardio-pulmonary resuscitation procedures of the clinic or hospital.
Mild allergic reactions should be managed by stopping the administration of Venofer and administering antihistamines. Hypotensive episodes may occur if the injection is administered too rapidly. Patients with low iron binding capacity and/or folic acid deficiency are particularly at risk of an allergic or anaphylactoid reaction.
In cases of inadvertent paravenous leakage, and if the needle is still inserted, rinse with a small amount of 0.9% sodium chloride solution.
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).
In patients with liver dysfunction, parenteral iron should only be administered after careful risk/benefit assessment. Parenteral iron administration should be avoided in patients with hepatic dysfunction where iron overload is a precipitating factor, in particular Porphyria Cutanea Tarda (PCT). Careful monitoring of iron status is recommended to avoid iron overload.

Pregnancy and lactation
Data on a limited number of exposed pregnancies indicated no adverse effects of Venofer on pregnancy or on the helth of the foetus/newborn child. No well-controlled studies in pregnant women ara available to date. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.
Nevertheless, risk/benefit evaluation is required. Venofer should only be used in pregnant women in whom oral iron is ineffective or cannot be tolerated and the level of anaemia is judged sufficient to put the mother or foetus at risk.
Pregnancy first trimester: see contraindications
Non metabolized Venofer is unlikely to pass into the mother's milk. No well-controlled clinical studies are available to date. Animal studies do not indicate direct or indirect harmful effects to the nursing child.

Effects on Ability to Drive and Use Machines
In the case of symptoms of dizziness, confusion or light headedness following the administration of Venofer, patients should not drive or use machinery until the symptoms have ceased.

Overdose
Overdosage can cause acute iron overloading which may manifest itself as haemosiderosis. Overdosage should be treated with supportive measures and, if required, an iron chelating agent.

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ID REG : EREG10021712300094

Interaction with other medicaments and other forms of interaction
As with all parenteral iron preparations, Venofer should not be administered concomitantly with oral iron preparation since the absorption of oral iron is reduced. Therefore, oral iron therapy should be started at least 5 days after the last injection of Venofer.

Posology
The cumulative dose of Venofer must be calculated for each patient individually and must not be exceeded.

Calculation of dosage
The total cumulative dose of Venofer, equivalent to the total iron deficit (mg), is determined by the hemoglobin level (Hb) and body weight (BW). The dose of Venofer must be individually calculated for each patient according to the total iron deficit calculated with the following Ganzoni formula, for example:

Total iron deficit [mg] = BW [kg] × (target Hb – actual Hb) [g/dl] × 2.4* + storage iron [mg]

Below 35 kg BW:
Target Hb = 13 g/dl and storage iron = 15 mg/kg BW

35 kg BW and above:
Target Hb = 15 g/dl and storage iron = 500 mg

*Factor 2.4 = 0.0034 (iron content of Hb = 0.34%) × 0.07 (blood volume = 7% of BW) × 1000 (conversion of [g] to [mg]) × 10

Total Venofer to be administered (in ml)
$= \frac{\text{Total iron deficit [mg]}}{\text{20 mg iron/ml}}$

Total amount of Venofer to be administered according to body weight, actual Hb level and target Hb level*:

BW	Total Venofer (20 mg iron per ml) to be administered			
	Hb 6.0 g/dl	Hb 7.5 g/dl	Hb 9.0 g/dl	Hb 10.5 g/dl
30 kg	47.5 ml	42.5 ml	37.5 ml	32.5 ml
35 kg	62.5 ml	57.5 ml	50 ml	45 ml
40 kg	67.5 ml	60 ml	55 ml	47.5 ml
45 kg	75 ml	65 ml	57.5 ml	50 ml
50 kg	80 ml	70 ml	60 ml	52.5 ml
55 kg	85 ml	75 ml	65 ml	55 ml
60 kg	90 ml	80 ml	67.5 ml	57.5 ml
65 kg	95 ml	82.5 ml	72.5 ml	60 ml
70 kg	100 ml	87.5 ml	75 ml	62.5 ml
75 kg	105 ml	92.5 ml	80 ml	65 ml
80 kg	112.5 ml	97.5 ml	82.5 ml	67.5 ml
85 kg	117.5 ml	102.5 ml	85 ml	70 ml
90 kg	122.5 ml	107.5 ml	90 ml	72.5 ml

*Below 35 kg BW : Target Hb = 13 g/dl
35 kg BW and above : Target Hb =15 g/dl

To convert Hb (mM) to Hb (g/dl), multiply the former by 1.6.
If the total necessary dose exceeds the maximum allowed single dose, then the administration must be divided. If no response of the hematological parameters is observed after 1 to 2 weeks, the original diagnosis should be reconsidered.

Posology
Adults
5–10 ml of Venofer (100–200 mg iron) 1 to 3 times a week.
For administration time and dilution ratio see "Method of administration".

Pediatric Patients (2 Years of Age and Older) with Hemodialysis Dependent-Chronic Kidney Disease (HDD-CKD) for Iron Maintenance Treatment
For iron maintenance treatment: Administer Venofer at a dose of 0.5 mg/kg, not to exceed 100 mg per dose, every two weeks for 12 weeks given undiluted by slow intravenous injection over 5 minutes or diluted in 0.9% NaCl at a concentration of 1 to 2 mg/mL and administered over 5 to 60 minutes. Do not dilute to concentrations below 1 mg/mL. Venofer treatment may be repeated if necessary.
The dosing for iron replacement treatment in pediatric patients with HDD-CKD has not been established.

Method of administration
Venofer must only be administered by the intravenous route. This may be a slow intravenous injection or by an intravenous drip infusion. However, administration by intravenous drip infusion is the preferred route of administration as this may help to reduce the risk of hypotensive episodes and paravenous leakage. Before administering the first dose to new patient, a test dose of Venofer should be given.
Facilities for cardio-pulmonary resuscitation must be available when administering Venofer because allergic or anaphylactoid reactions and hypotensive episodes may occur.
Venofer is a strongly alkaline solution, and must never be administered by the subcutaneous or intramuscular route. Paravenous leakage must be avoided because leakage of Venofer at the injection site may lead to pain, inflammation, tissue necrosis, sterile abscess, and brown discoloration of the skin.

Intravenous drip infusion
Venofer must only be diluted in sterile 0.9% m/V sodium chloride (NaCl) solution. Dilution must take place immediately prior to infusion and the solution should be administered as follows:

Venofer dose (mg of iron)	Venofer dose (ml of Venofer)	Maximum dilution volume of sterile 0.9% m/V NaCl solution	Minimum infusion time
50 mg	2.5 ml	50 ml	8 minutes
100 mg	5 ml	100 ml	15 minutes
200 mg	10 ml	200 ml	30 minutes

For stability reasons, dilution to lower Venofer concentrations are not permissible.

Intravenous injection
Venofer must be administered by slow intravenous injection at a rate of 1 ml undiluted solution per minute and not exceeding 10 ml (200 mg iron) per injection.

Injection into venous line of dialysis machine
Venofer may be administered during a hemodialysis session directly into the venous line of the dialysis machine under the same conditions as for intravenous injection.

Incompatibilities
Venofer must only be mixed with 0.9% of sodium chloride solution. No other intravenous dilution solutions and therapeutics agents should be used as there is the potential for the precipitation and/or interaction. The compatibility with containers other than glass, polyethylene and PVC is not known.

Shelf life
Shelf life in the product as packaged for sale is 2 years.

Shelf life after first opening the container:
From a microbiological point of view, the product should be used immediately.

Shelf life after dilution with 0.9% sodium chloride solution:
Chemical and physical in-use stability has been demonstrated for 12 hours at room temperature. From a microbiological point of view, the product should be used immediately.

Special precautions for storage
Store in original carton. Store below 30°C.
Do not freeze.

Instruction for use/handling
Ampoules should be visually inspected for sediment and damage before use. Only those with sediment free and homogenous solution must be used.
See also shelf life.

Package form
Ampoules (5 mL) containing 100 mg of iron: 5

Reg. No. DKI0355200143A1

Manufactured by:
Siegfried Hameln GmbH
Langes Feld 13
31789 Hameln
Germany

For:
Vifor (International) Inc.
St. Gallen, Switzerland

Imported by:
PT. COMBIPHAR
Bandung Barat, Indonesia

HARUS DENGAN RESEP DOKTER
ON MEDICAL PRESCRIPTION ONLY

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