**Summary of Product Characteristics for Pharmaceutical Products**

## 1. Name of the medicinal product:

HEMOFLUX 50mg iron/ml dispersion for injection/infusion.

## 2. Qualitative and quantitative composition

One ml of dispersion contains ferric carboxymaltose corresponding to 50 mg iron.

Each ampoule contains 10 ml sterile solution of Ferric Carboxymaltose corresponding to 500mg Elemental Iron (50 mg/ml)

For the full list of excipients, see section 6.1.

## 3. Pharmaceutical form

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

## 4. Clinical particulars

### 4.1 Therapeutic indications

Ferric Carboxymaltose indicated for the treatment of iron deficiency anemia in adult patient:

- Who have intolerance to oral iron or have had unsatisfactory response to oral iron.
- Who have no-dialysis dependent chronic kidney disease.
- There is a clinical need to deliver iron rapidly.

The diagnosis of iron deficiency must be based on laboratory tests.

### 4.2 Posology and method of administration

Monitor carefully patients for signs and symptoms of hypersensitivity reactions during and following each administration of Hemoflux. Hemoflux 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. The patient should be observed for adverse effects for at least 30 minutes following each Hemoflux administration (see section 4.4).

<u>Posology</u>

The posology of Ferric Carboxymaltose follows a step wise approach
(1) Determination of the Individual iron need,
(2) Calculation and administration of the iron dose(s), and
(3) Post-iron repletion assessments.
These steps are outlined below:

**Step 1: Determination of the iron need**
The individual iron need for repletion using Feritol-Q is determined based on the patient's body weight and haemoglobin (Hb) level. Refer to Table 1 for determination of the total iron need. 2 doses may be required to replenish the total iron need, see Step 2 for the maximum individual iron doses.

Iron deficiency must be confirmed by laboratory tests as stated in section 4.1.

Table 1: Determination of the Iron need

| **Hb** | | **Patient body weight** | | |
|---|---|---|---|---|
| **g/dL** | **mmol/L** | **below 35 kg** | **35 kg to <70 kg** | **70 kg and above** |
| <10 | <6.2 | 30 mg/kg body weight | 1,500 mg | 2,000 mg |
| 10 to <14 | 6.2 to <8.7 | 15 mg/kg body weight | 1,000 mg | 1,500 mg |
| ≥ 14 | ≥ 8.7 | 15 mg/kg body weight | 500 mg | 500 mg |

**Step 2: Calculatlon and administration of the maximum individual Iron dose(s)**
Based on the total iron need determined, the appropriate dose(s) of Hemoflux should be administered taking into consideration the following:

**Adults and adolescents aged 14 years and older**

A single Hemoflux administration should not exceed:

• 15 mg iron/kg body weight (for administration by intravenous injection) or 20 mg iron/kg body weight (for administration by intravenous infusion)

• 1,000 mg of iron (20 ml Hemoflux)

The maximum recommended cumulative dose of Hemoflux is 1,000 mg of iron (20 ml Hemoflux) per week. If the total iron need is higher, then the administration of an additional dose should be a minimum of 7 days apart from the first dose.

**Children and adolescents aged 1 to 13 years**

A single Hemoflux administration should not exceed:

• 15 mg iron/kg body weight

• 750 mg of iron (15 ml Hemoflux)

The maximum recommended cumulative dose of Hemoflux is 750 mg of iron (15 ml Hemoflux) per week. If the total iron need is higher, then the administration of an additional dose should be a minimum of 7 days apart from the first dose.

**Step 3: Post-iron repletion assessments**
Re-assessment should be performed by the clinician based on the individual patient's condition. The Hb level should be re-assessed no earlier than 4 weeks post final Hemoflux administration to allow adequate time for erythropoiesis land iron utilization, In the event the patient requires further iron repletion, the iron need should be recalculated using Table 1 above.

**Children below 1 year of age**
The efficacy and safety of Hemoflux has not been investigated in children below 1 year of age. Hemoflux is therefore not recommended for use in children in this age group.

**Patients with haemodialysis-dependent chronic kidney disease**
In adults and adolescents aged 14 years and older, a single maximum daily dose of 200 mg iron should not be exceeded in haemodialysis-dependent chronic kidney disease patients (see also section 4.4).
In children aged 1 to 13 years with chronic kidney disease requiring haemodialysis, the efficacy and safety of Hemoflux has not been investigated. Hemoflux is therefore not recommended for use in children aged 1 to 13 years with chronic kidney disease requiring haemodialysis.

Method of administration

Hemoflux must only be administered by the intravenous route:

- by injection, or
- by infusion, or
- during a haemodialysis session undiluted directly into the venous limb of the dialyser.

Hemoflux must not be administered by the subcutaneous or intramuscular route.

*Intravenous injection*

Hemoflux may be administered by intravenous injection using undiluted dispersion. In adults and adolescents aged 14 years and older, the maximum single dose is 15 mg iron/kg body weight but should not exceed 1,000 mg of iron. In children aged 1 to 13 years, the maximum single dose is 15 mg iron/kg body weight but should not exceed 750 mg of iron. The administration rates are as shown in Table 2:

**Table 2: Administration rates for intravenous injection of Hemoflux**

| **Volume of Hemoflux required** | **Equivalent iron dose** | **Administration rate / Minimum administration time** |
|---|---|---|
| 2 to 4 ml | 100 to 200 mg | No minimal prescribed time |
| >4 to 10 ml | >200 to 500 mg | 100 mg iron / min |
| >10 to 20 ml | >500 to 1,000 mg | 15 minutes |

Intravenous infusion

Hemoflux may be administered by intravenous infusion, in which case it must be diluted. In adults and adolescents aged 14 years and older, the maximum single dose is 20 mg iron/kg body weight but should not exceed 1,000 mg of iron. In children aged 1 to 13 years, the maximum single dose is 15 mg iron/kg body weight but should not exceed 750 mg of iron.

For infusion, Hemoflux must only be diluted in sterile 0.9% m/V sodium chloride solution as shown in Table 3.

Note: for stability reasons, Hemoflux should not be diluted to concentrations less than 2 mg iron/ml (not including the volume of the ferric carboxymaltose dispersion). For further instructions on dilution of the medicinal product before administration, see section 6.6.

**Table 3: Dilution plan of Hemoflux for intravenous infusion**

| **Volume of Hemoflux required** | **Equivalent iron dose** | **Maximum amount of sterile 0.9% m/V sodium chloride solution** | **Minimum administration time** |
|---|---|---|---|
| 2 to 4 ml | 100 to 200 mg | 50 mL | No minimal prescribed time |
| >4 to 10 ml | >200 to 500 mg | 100 mL | 6 minutes |
| >10 to 20 ml | >500 to 1,000 mg | 250 mL | 15 minutes |

## 4.3 Contraindications

The use of Hemoflux is contraindicated in cases of:

• Hypersensitivity to the active substance, to Ferric Carboxymaltose or any of its excipients
• Known serious Hypersensitivity to other parenteral iron products
• Anaemia not attributed to iron deficiency, e.g. other microcytic anaemia
• Evidence of iron overload or disturbances in the utilization of iron

## 4.4 Special warnings and precautions for use

Hypersensitivity reactions

Parenterally administered iron preparations can cause hypersensitivity reactions, including serious and potentially fatal anaphylactic reactions. Hypersensitivity reactions have also been reported after previously uneventful doses of parenteral iron complexes. There have been reports of hypersensitivity reactions which progressed to Kounis syndrome (acute allergic coronary arteriospasm that can result in myocardial infarction, see section 4.8).

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).

Hemoflux should only be administered when staff trained to evaluate and manage anaphylactic reactions are 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 Hemoflux administration. 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 reactions should be available, including an injectable 1:1000 adrenaline solution. Additional treatment with antihistamines and/or corticosteroids should be given as appropriate.

Hypophosphataemic osteomalacia

Symptomatic hypophosphataemia leading to osteomalacia and fractures requiring clinical intervention, including surgery has been reported in the post-marketing setting. Patients should be asked to seek medical advice if they experience worsening fatigue with myalgias or bone pain. Serum phosphate should be monitored in patients who receive multiple administrations at higher doses or long-term treatment, and those with existing risk factors for hypophosphataemia. In case of persisting hypophosphataemia, treatment with ferric carboxymaltose should be re-evaluated.

Hepatic or renal impairment

In patients with liver dysfunction, parenteral iron should only be administered after careful benefit/risk 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.

No safety data on haemodialysis-dependent chronic kidney disease patients receiving single doses of more than 200 mg iron are available.

Infection

Parenteral iron must be used with caution in case of acute or chronic infection, asthma, eczema or atopic allergies. It is recommended that the treatment with Hemoflux is stopped in patients with ongoing bacteraemia. Therefore, in patients with chronic infection a benefit/risk evaluation has to be performed, taking into account the suppression of erythropoiesis.

Extravasation

Caution should be exercised to avoid paravenous leakage when administering Hemoflux. Paravenous leakage of Hemoflux at the administration site may lead to irritation of the skin and potentially long-lasting brown discolouration at the site of administration. In case of paravenous leakage, the administration of Hemoflux must be stopped immediately.

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

The absorption of oral iron is reduced when administered concomitantly with parenteral iron preparations. Therefore, if required, oral iron therapy should not be started for at least 5 days after the last administration of Hemoflux.

## 4.6 Pregnancy and Lactation

**Pregnancy**

There are limited data from the use of Hemoflux in pregnant women. A careful benefit/risk evaluation is required before use during pregnancy and Hemoflux should not be used during pregnancy unless clearly necessary.

Iron deficiency occurring in the first trimester of pregnancy can in many cases be treated with oral iron. Treatment with Hemoflux should be

confined to the second and third trimester if the benefit is judged to outweigh the potential risk for both the mother and the foetus.

Foetal bradycardia may occur following administration of parenteral irons. It is usually transient and a consequence of a hypersensitivity reaction in the mother. The unborn baby should be carefully monitored during intravenous administration of parenteral irons to pregnant women.

Animal data suggest that iron released from Hemoflux can cross the placental barrier and that its use during pregnancy may influence skeletal development in the foetus (see section 5.3).

**Lactation**

Based on limited data on breast-feeding women, it is unlikely that Hemoflux represents a risk to the breast-fed child.

## 4.7 Effects on ability to drive and use machines

Hemoflux is unlikely to impair the ability to drive and use machines.

## 4.8 Undesirable effects

The most commonly reported ADR is nausea, followed by injection/infusion site reactions, hypophosphataemia, headache, flushing, dizziness and hypertension. Injection/infusion site reactions comprise several ADRs, which individually are either uncommon or rare.

The most serious ADR is anaphylactic reactions (rare); fatalities have been reported. See section 4.4 for further details.

**Table 4: Adverse drug reactions observed**

| **System Organ Class** | **Common (≥ 1/100 to <1/10)** | **Uncommon (≥ 1/1,000 to <1/100)** | **Rare (≥ 1/10,000 to <1/1,000)** | **Freque known** |
|---|---|---|---|---|
| **Immune system disorders** | | Hypersensitivity | Anaphylactic reactions | |
| **Metabolism and nutritional disorders** | Hypophosphataemia | | | |
| **Nervous system disorders** | Headache, dizziness | Dysgeusia, paraesthesia | | Loss of conscio |
| **Psychiatric disorders** | | | Anxiety[2] | |

| | | | | |
|---|---|---|---|---|
| **Cardiac disorders** | | Tachycardia | | Kounis |
| **Vascular disorders** | Flushing, hypertension | Hypotension | Presyncope[2], syncope[2], phlebitis | |
| **Respiratory, thoracic and mediastinal disorders** | | Dyspnoea | Bronchospasm[2] | |
| **Gastrointestinal disorders** | Nausea | Abdominal pain, vomiting, constipation, diarrhoea, dyspepsia | Flatulence | |
| **Skin and subcutaneous tissue disorders** | | Rash[3], pruritus, urticaria, erythema | Angioedema[2], distant skin discolouration[2], pallor[2] | Face oe |
| **Musculoskeletal and connective tissue disorders** | | Arthralgia, myalgia, pain in extremity, back pain, muscle spasms | | Hypoph osteom |
| **General disorders and administration site conditions** | Injection/infusion site reactions[4] | Pyrexia, fatigue, chills, chest pain, oedema peripheral, malaise | Influenza like illness (whose onset may vary from a few hours to several days) [2] | |
| **Investigations** | | Alanine aminotransferase increased, aspartate aminotransferase increased, gamma-glutamyltransferase increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased | | |

**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 Pharmacy and Poisons board Pharmacovigilance Electronic Reporting System(PvERS)

Website: https://pv.pharmacyboardkenya.org

## 4.9 Overdose

Excessive dosages of Ferric Carboxymaltose may lead to accumulation of iron in storage sites potentially leading to hemosiderosis. Monitoring of iron parameters such as serum ferritin and transferrin saturation(TSAT) may assist in recognizing iron accumulation. If iron accumulation has occurred, treat according to standard medical practice, e.g. consider the use of an iron chelator

# 5. Pharmacological properties

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Iron trivalent, parenteral preparation,

ATC code: B03AC

Hemoflux dispersion for injection/infusion is a colloidal solution of the iron complex ferric carboxymaltose.

The complex is designed to provide, in a controlled way, utilisable iron for the iron transport and storage proteins in the body (transferrin and ferritin, respectively).

Red cell utilisation of 59Fe from radio-labelled Hemoflux ranged from 91% to 99% in subjects with iron deficiency (ID) and 61% to 84% in subjects with renal anaemia at 24 days post-dose.

Hemoflux treatment results in an increase in reticulocyte count, serum ferritin levels and TSAT levels to within normal ranges.

## 5.2 Pharmacokinetic properties

### Distribution

Positron emission tomography demonstrated that 59Fe and 52Fe from Hemoflux was rapidly eliminated from the blood, transferred to the bone marrow, and deposited in the liver and spleen.

After administration of a single dose of Hemoflux of 100 to 1,000 mg of iron in ID subjects, maximum total serum iron levels of 37 µ g/ml up to 333 µ g/ml are obtained after 15 minutes to 1.21 hours, respectively. The volume of the central compartment corresponds well to the volume of the plasma (approximately 3 litres).

**Elimination**

The iron injected or infused was rapidly cleared from the plasma, the terminal half-life ranged from 7 to 12 hours, the mean residence time (MRT) from 11 to 18 hours. Renal elimination of iron was negligible.

**Paediatric population**

The pharmacokinetic properties of Hemoflux at a dose of 15 mg iron/kg were similar to those for adult patients with iron deficiency. Serum iron increased proportionally to the dose after a single dose of 7.5 mg iron/kg or 15 mg iron/kg. After a single dose of Hemoflux of 15 mg iron/kg body weight (maximum 750 mg), average maximum total serum iron values of 310 µ g/ml were measured after 1.12 hours. The terminal half-life was 9.8 hours, and the distribution volume estimated by the population pharmacokinetic analysis was 0.42 to 3.14L. Based on model-based simulations, the paediatrics subjects tended to have lower systemic exposure (lower AUC0-72h) compared to the adults (median per age group: 3,340 µ g× h/mL (1 to 2 years), 4,110 µ g× h/mL (3 to 12 years), 4,740 µ g× h/mL (13 to 17 years), 8,864 µ g× h/mL (adults)).

## 5.3 Preclinical safety data

Preclinical data revealed no special hazard for humans based on conventional studies of safety pharmacology, repeat dose toxicity and genotoxicity. Preclinical studies indicate that iron released from Hemoflux does cross the placental barrier and is excreted in milk in limited, controlled amounts. In reproductive toxicology studies using iron replete rabbits Hemoflux was associated with minor skeletal abnormalities in the foetus. In a fertility study in rats, there were no effects on fertility for either male or female animals. No long-term studies in animals have been performed to evaluate the carcinogenic potential of Hemoflux. No evidence of allergic or immunotoxic potential has been observed. A controlled in vivo test demonstrated no cross-reactivity of Hemoflux with anti-dextran antibodies. No local irritation or intolerance was observed after intravenous administration.

# 6. Pharmaceutical Particulars

## 6.1 List of Excipients

Water for injection

## 6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.
The compatibility with containers other than polyethylene and glass is not known.

## 6.3 Shelf-Life

*Shelf life of the product as packaged for sale:*
2 years.

*Shelf life after first opening of the container:*
From a microbiological point of view, preparations for parenteral administration should be used immediately.

*Shelf life after dilution with sterile 0.9% m/V sodium chloride solution:*
From a microbiological point of view, preparations for parenteral administration should be used immediately after dilution with sterile 0.9% m/V sodium chloride solution.

**6.4 Special Precautions for storage**

Store in the original package in order to protect from light. Do not store above 30 ° C. Do not freeze.

**6.5 Nature and Content of container**

Hemoflux is supplied in a vial (type I glass) with a stopper (bromobutyl rubber) and an aluminium cap containing:
– 10 mL dispersion. Pack sizes of 1, 2 or 5 vials.

**6.6 Special precautions for disposal and other handling**

Inspect vials visually for sediment and damage before use. Use only those containing sediment-free, homogeneous dispersion.
Each vial of Hemoflux is intended for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.
Hemoflux must only be mixed with sterile 0.9% m/V sodium chloride solution. No other intravenous dilution solutions and therapeutic agents should be used, as there is the potential for precipitation and/or interaction. For dilution instructions.

**7. Marketing Authorization Holder**

Dawa Limited,
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P.O Box 16633-00620, Nairobi -Kenya

**8. Marketing Authorization Number**

CTD11092

**9. Date of first authorization/renewal of the authorization**

01/08/2024

## 10. Date of revision of the text

11/05/2025