Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product:

FERITOL-Q 500 IV INJECTION 10 ML

2. Qualitative and quantitative composition

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

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Injection

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 Feritol-Q.
Feritol-Q 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 Feritol-Q administration (see section 4.4).

Posology

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 Feritol-Q should be administered taking into consideration the following:

Adults and adolescents aged 14 years and older

A single Feritol-Q 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 Feritol-Q)

The maximum recommended cumulative dose of Feritol-Q is 1,000 mg of iron (20 ml Feritol-Q) 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 Feritol-Q administration should not exceed:

• 15 mg iron/kg body weight

• 750 mg of iron (15 ml Feritol-Q)

The maximum recommended cumulative dose of Feritol-Q is 750 mg of iron (15 ml Feritol-Q) 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 Feritol-Q 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 Feritol-Q has not been investigated in children below 1 year of age. Feritol-Q 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 Feritol-Q has not been investigated. Feritol-Q is therefore not recommended for use in children aged 1 to 13 years with chronic kidney disease requiring haemodialysis.

Method of administration

Feritol-Q 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.

Feritol-Q must not be administered by the subcutaneous or intramuscular route.

Intravenous injection

Feritol-Q 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 Feritol-Q

Volume of Feritol-Q 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

Feritol-Q 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, Feritol-Q must only be diluted in sterile 0.9% m/V sodium chloride solution as shown in Table 3.

Note: for stability reasons, Feritol-Q 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 Feritol-Q for intravenous infusion

Volume of Feritol-Q 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 Feritol-Q 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).

Feritol-Q 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 Feritol-Q 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 Feritol-Q 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 Feritol-Q. Paravenous leakage of Feritol-Q 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 Feritol-Q 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 Feritol-Q.

4.6 Pregnancy and Lactation

Pregnancy

There are limited data from the use of Feritol-Q in pregnant women. A careful benefit/risk evaluation is required before use during pregnancy and Feritol-Q 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 Feritol-Q 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 Feritol-Q 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 Feritol-Q represents a risk to the breast-fed child.

4.7 Effects on ability to drive and use machines

Feritol-Q 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 osteoma
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

Feritol-Q 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 Feritol-Q 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.

Feritol-Q 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 Feritol-Q 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 Feritol-Q 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 Feritol-Q 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 Feritol-Q 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 Feritol-Q does cross the placental barrier and is excreted in milk in limited, controlled amounts. In reproductive toxicology studies using iron replete rabbits Feritol-Q 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 Feritol-Q. No evidence of allergic or immunotoxic potential has been observed. A controlled in vivo test demonstrated no cross-reactivity of Feritol-Q 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

Not applicable

6.3 Shelf-Life

Two years from the date of manufacturing when it is kept in original pack

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

Primary packaging

• 10 ml amber Ampoule, type I glass with green breaking line

Secondary packaging

• Consists of Alu-PVC (clear) blister pack, Sticker label, Unit carton, Insert, Hologram sticker (Transparent with logo, VOID) and Master Carton.

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.

For storage conditions after dilution or first opening of the medicinal product, see section 6.3.

Each vial of Feritol-Q is intended for single use only. Any unused product or waste material should be disposed of in accordance with local requirements.

Feritol-Q 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, see section 4.2.

7. Marketing Authorization Holder

GENERAL Pharmaceuticals Ltd.
Sara Aftab Tower, 29 Ring Road (Holding # 6/1/A),
Shyamoli, Adabor, Dhaka- 1207,
Bangladesh.

8. Marketing Authorization Number

CTD11164

9. Date of first authorization/renewal of the authorization

10/9/2024

10. Date of revision of the text

08/05/2024