National Agency for Food & Drug Administration & Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

BECKARON BLOOD TONIC

1. NAME OF THE MEDICINAL PRODUCT

Beckaron Blood Tonic

(Ferric ammonium citrate, Folic acid, and Vit B12)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains:

Ferric Ammonium Citrate	USP 200 mg
(Equivalent to Elemental Iron 41 mg)	
Folic Acid	USP 1.5 mg
Vitamin B12	BP 50 mcg

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

A red coloured and fruity viscous liquid syrup.

4. Clinical particulars

4.1 Therapeutic indications

Treatment of iron deficiency anaemia. It is essential to make an accurate diagnosis before starting treatment.

Treatment preventing iron and folic acid deficiencies in case of low dietary iron and folic acid supplementation.

Prevention of neural tube defects with folic acid is recommended before conception and during the first trimester of pregnancy

4.2 Posology and method of administration

Posology

The posology and the period of treatment depends on the level of iron deficiency.

	Posology for Iron supplement		Posology for severe anaemia	
Age	Qty of Iron mg/day	Qty of Beckaron ml/day	Qty of Iron mg/day during 3 months	Qty of Beckaron ml/day
Children 1 – 13 years	30 mg	5 ml		
Adolescents 14 –18 year	60 mg	10 ml	120 mg	20 ml
Adults ≥ 19 year	60 mg	10 ml	120 mg	20 ml
Pregnancy & breast feeding	60 mg	10 ml	120 mg	20 ml

Method of administration

Oral use by means of a dosing device. Shake the bottle well before each use.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients.

- Conditions with high serum iron levels (hemochromatosis, hypersiderosis, chronic hemolysis)
- All forms of anemia in the absence of a confirmed iron deficiency origin. For example, megaloblastic anemia resulting from isolated vitamin B12 deficiency (e.g., an intrinsic factor deficiency), and an isolated folic acid deficiency.
- In case of problems inherent to iron consumption (anemia of lead poisoning, sideroblastic anemia).
- In case of thalassemia.
- In case of degenerative or chronic arthritis
- In case of conditions requiring frequent and continuous blood transfusions
- In case of HIV infection without anemia due to iron deficiency highlighted by clinical measures.
- In case of severe liver or kidney problems.

4.4 Special warnings and precautions for use

- Oral iron preparations are used with caution in patients with gastritis, gastric or intestinal ulcer, Crohn's disease and ulcerative colitis.
- Caution is exercised in cases of chronic alcohol abuse, as it can cause iron overload through increased iron resorption.
- Additional administration of folic acid may be required during hemolytic anemia, chronic infections, anticonvulsive therapies or alcoholism.
- Additional parenteral administration of cyanocobalamin may be necessary for vitamin B12 deficiency.
- A dark coloration of the stools can occur during the treatment with Ferrol Plus syrup, however it is not clinically relevant.
- If treatment is ineffective, resulting in an increase in hemoglobin levels of about 0.1g/dL of blood per day (about 2 to 3 g/dL in 3 weeks), treatment should be reviewed.
- In case of anemia associated with an infection or malignant tumor, the iron administered is stored in the reticulo-endothelial system and is used during mobilisation after treatment of the primary condition.

Paediatric population

For infants and children who solemnly need treatment with an iron supplement, sole-ingredient iron syrup (as iron-hydroxide-polymaltose complex).

4.5 Interaction with other medicinal products and other forms of interaction

- Compounds containing Calcium and Magnesium including antacids and mineral supplements and bicarbonates, carbonates, oxalates or phosphates, may also impair the absorption of iron by the formation of insoluble complexes.

- Similarly absorption of both iron & tetracyclines is diminished when they are taken concomitantly by mouth. If treatment with both drugs is required, a time interval of about 2 to 3 hours should be allowed between them.
- Avoid milk and dairy products at least for 2 hours.
- Some agents such as Ascorbic Acid & Citric Acid may actually increase the absorption of iron.
- The response to iron may be delayed in patients receiving concomitant parenteral chloramphenicol therapy.
- Iron salts can decrease the absorption of bisphosphonates, fluoroquinolones, levodopa, methyldopa, penicillamine and tetracycline. Iron salts may reduce the efficacy of thyroxine.

4.6 Pregnancy and Lactation

- Can be used in Iron deficiency anaemia during Pregnancy and Lactation after considering risk benefit ratio.
- It is not known whether ferric ammonium citrate passes into breast milk.
- The excretion does not change the mother's iron content and the amount of iron consumed with food. As a result, the administration of formulations of iron to the lactating mother does not cause iron poisoning in the baby and does not eliminate an existing iron deficiency in the baby

4.7 Effects on ability to drive and use machines

No known effects

4.8 Undesirable effects

The table below describes adverse events according to the MedDRA classification. Adverse effects reported from the experience since the introduction of folic acid and iron preparations.

Reported side effects are defined as:

- very common ≥1/10
- common ≥1/100 and ≥1/10
- uncommon ≥1/1000 and <1/100
- rare ≥1/10000 and <1/1000
- very rare <1/10000
- not known: (cannot be estimated from the available data)

System organ class	Undesirable effect	Frequency
Immune system disorders	Anaphylactic reaction Hypersensibility	Not known
Gastrointestinal disorders	Abdominal disorders Diarrhoea Constipation Dark colouring of the faeces (1) Vomiting	Not known
Skin and subcutaneous tissue disorders	Angioedema (face) Allergic skin reactions such as generalised rash, rash, pruritus, hives, skin edema, photosensitivity reaction	Not known (2)

(1) Dark colouring of the faeces is a well-known side effect of iron-based oral preparations but is not considered clinically relevant and is often not reported.

(2) Hypersensitivity reactions induced by folic acid have been reported a few times in the literature: anaphylactic reaction, swelling of the face, vomiting and allergic skin reactions (generalised erythema, pruritus, hives). Iron-based oral preparations are also associated with hypersensitivity reactions such as anaphylactic reactions and allergic skin reactions (rash, pruritus, hives, skin oedema and photosensitivity).

4.9 Overdose

The most sign & Symptoms of overdosage are Gastrointestinal irritation, abdominal pain with nausea, vomiting and either diarrhoea or constipation. Cardiovascular disorders such as hypotension, tachycardia, metabolic changes including acidosis and hypoglycemia.

CNS depression ranging from lethargy to coma.

Vomiting is induced immediately followed by parenteral injection of desferroxamine mesylate and then gastric lavage. In the meantime, give milk and/or 5% sodium bicarbonate solution by mouth. Fluid replacement is essential. Other measures include symptomatic management and therapy of metabolic and cardiovascular disorders.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Antianemic, ATC code: B03AE01

Ferric ammonium citrate

Ferric ion is a component of many enzymes necessary for energy transfer (cytochrome oxidase, xanthine oxidase, and succinic dehydrogenase), and it is also present in compounds necessary for the transfer and

use of oxygen (haemoglobin and myoglobin). Administration of iron preparations corrects erythropoietic abnormalities arising from iron deficiency. Iron also eliminates other iron deficiency symptoms such as tongue sores, dysphagia, nail and skin dystrophy, and cracking of the lips.

Folic acid

In humans, an exogenous source of folic acid is needed for nucleoprotein synthesis and maintenance of normal erythropoiesis. Folic acid is not metabolically active as such, but as a precursor of tetrahydrofolic acid acting as a cofactor for the transfer of 1-carbo reactions in the biosynthesis of purines and thymidylates of nucleic acids. The decreased thymidylate synthesis in patients with folic acid deficiency appears to be responsible for failing DNA synthesis that leads to megaloblastic formation and megaloblastic and macrocytic anaemia.

Cyanocobalamin (vitamin B12)

In humans, an exogenous source of vitamin B12 is required for nucleoprotein and myelin synthesis, cell reproduction, normal growth, and maintenance of normal erythropoiesis. Cells with rapid division (epithelial cells, myeloid cells, bone marrow cells) seem to require more vitamin B12 intake. Vitamin B12 would be converted to coenzyme B12 in tissues, and this is essential for the conversion of methylmalonate to succinate and the synthesis of methionine from homocysteine, a reaction that also requires folate.

In the absence of coenzyme B12, the regeneration of tetrahydrofolate from its inactive form 5methyl tetrahydrofolate is impossible, resulting in a functional folate deficiency.

Vitamin B12 would also be needed for the maintenance of reduced sulfhydryl (SH) groups required in several activated SH enzyme systems. Apart from these reactions, vitamin B12 is also associated with the metabolism of fats and carbohydrates, and with the synthesis of proteins.

Vitamin B12 deficiency leads to megaloblastic anaemia, gastrointestinal damage and neurological damage that begins with an inability to produce myelin, and then follows a gradual degeneration of the axon and nerve head. Parenteral administration of vitamin B12 completely reverses megaloblastic anaemia and gastrointestinal symptoms of vitamin B12 deficiency. The degree of improvement in neurological symptoms depends on the duration and severity of the lesions, although progression of the lesions is immediately stopped.

5.2 Pharmacokinetic properties

Ferric ammonium citrate

Absorption

Iron absorption is very complex and is influenced by several factors including the form in which it is administered, the dose, the iron reserve, the erythroid degree and diet. In healthy subjects, approximately 5-10% of dietary iron is absorbed, and almost 10- 30% in iron deficient subjects. It is reported that inorganic iron is absorbed twice as much as dietary iron.

The ferric form Fe++ is the most absorbable. Although iron absorption occurs all along the gastrointestinal tract, it is more important in the duodenum, in the proximal portion of the jejunum, and decreases progressively in the distal portion. Some enteric preparations and sustained-release preparations may release iron after the duodenum and proximal jejunum, reducing the absorption of iron.

Distribution

Ferric iron Fe++ passes through the lining of the gastrointestinal tract directly into the blood and is immediately linked to the carriers. The β1-globulin transporter transports iron to bone marrow where it is incorporated into haemoglobin. Iron is found in the human body only in a complexed forms with a protein or in the haem- molecules. Approximately 70% iron is found in haemoglobin, 25% as ferritin iron, and haemosiderin, 4% in myoglobin, 0.5% in haemenzymes and 0.1% in transporters.

Iron stores in the form of ferritin and hemosiderin are localized in the liver, the reticuloendothelial system, bone marrow and in the spleen. In women, iron stocks tend to be less than half those of man. In patients with a negative iron balance, the iron stores decrease before the haemoglobin concentration is reduced.

Every day, almost 0.15 - 0.3 mg of iron is excreted in breast milk. Iron is transported through the placenta by the active route because it is against a concentration gradient. The iron requirement for a pregnant woman is between 440 mg and 1.05 g. Every day, iron excretion in a healthy woman, rises only up to 0.5 - 2 mg. This excretion appears mainly as a cellular desquamation such as skin, gastrointestinal mucosa, nails, and hair. Only traces of iron are eliminated in the bile and sweat. The loss of blood is accompanied by a great loss of iron. Each month, iron loss during normal menstruation amounts to 12 - 30 mg.

Elimination

The large amount of iron emanating from the destruction of haemoglobin is conserved and reused by the body.

Folic acid

Absorption

Folic acid is absorbed rapidly from the gastrointestinal tract after oral administration. Folic acid is mainly absorbed in the proximal portion of the small intestine. Naturally, the folate polyglutamates that appear are hydrolysed in the gastrointestinal tract, into monoglutamate forms of folic acid prior to absorption.

After oral administration, the maximal activity of the folates in the blood is reached in 30 - 60 min. Normal total folate concentrations in serum have been reported, ranging from 0.005 - 0.015 µg / ml. In general, folate serum concentrations below 0.005 µg / ml indicate folate deficiency and concentrations below 0.002 µg / ml are accompanied by megaloblastic anaemia.

Distribution

Tetrahydrofolic acid and its derivatives are distributed in all body tissues; the liver contains almost half of the total serum folate reserves. Folate is actively concentrated in CFS, and normal concentrations of CFS have been reported, ranging from 0.016 to 0.021 µg / ml. Normal erythrocyte folate concentrations vary between 0.175 - 0.316 µg / ml. Folic acid is distributed in the milk.

Elimination

After absorption folic acid is largely methylated in the liver to N5- methyltetrahydrofolic, the main transport and storage form of folate in the body.

After administration of large doses, some folic acid may escape hepatic metabolism, and appear in the blood mainly as folic acid.

After an administration of approximately 2.5 - 5.0 mg, almost 50% of the dose is excreted in the urine. Small doses of folic acid administered orally were found in the stool. Each day, about 0.05 mg of normal body folate storage is eliminated both urinary and faecal as well as by oxidative cleavage of the molecule.

Cyanocobalamin

Absorption

After oral administration, vitamin B12 is irregularly absorbed from the distal portion of the small intestine. Dietary vitamin B12 has a high degree of protein binding, and this binding must be broken down by proteolysis and gastric acid before absorption. In the stomach, free vitamin B12 is linked to the Intrinsic Factor (IF) secreted by the gastric mucosa. This binding is necessary for active absorption of vitamin B12 at the level of the lower ileum. In case of structural or functional damage of the stomach or ileum, the absorption of vitamin B12 is reduced.

After oral administration, the peak plasma is reached only after 8 to 12 hours because vitamin B12 is temporally retained in the wall of the lower ileum. Normal serum concentrations of VitB12 are between 200 - 900 µg/ml. In general, serum vitamin B12 concentrations below 200 pg/ml indicate vitally B12 deficiency, and concentrations below 100 pg / ml cause megaloblastic anaemia and / or neurological

Distribution

In intestinal mucosal cells, Vit-B12 is released from the Vit-B12-FI complex and rapidly binds to transport plasma proteins: transcobalamin. Vit B12 is distributed in the liver, bone marrow and other tissues, including the placenta. At birth, the blood vitamin B12 concentration in the newborn is 3 to 5 times higher than in the mother. Vit-B12 is found in breast milk at a concentration approaching that of vitamin B12 in the blood. The total body reserves of Vit-B12 in a healthy individual vary between 1 and 11 mg, of which 50-90% are concentrated in the liver

Elimination

In healthy subjects receiving only alimentary vitamin B12, almost 3 - 8 µg/ day of Vit- B12 is secreted in the gastrointestinal tract, mainly through the bile with a reabsorption of almost 1 µg. Less than 0.25 µg passes into the urine daily.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium propyl paraben, sorbitol, sodium hydroxide pellets, raspberry flavor, caramel, sodium methyl paraben, sugar.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store below 30^{o}C in a dry place. Keep all medicines out of reach of children

6.5 Nature and contents of container

A red coloured and fruity viscous liquid syrup in an Amber coloured Pet bottle, closed with a screw-ROPP cap. Box with 200ml syrup, with a plastic graduated measuring cup and leaflet.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER

Marketing authorisation holder

Highclout Pharma Limited
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Idi – Oro, Mushin,
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Manufacturer

Sagar Vitaceuticals Nigeria Limited
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