	Biomedical Limited, 1, Ohimege Road, Industrial Estate, Ga-Imam, Ilorin, Kwara State		
	Doc No. BML/FLX/S009	**Date rev 09/2020**	**Next rev date: 08/2025**

Summary of Product Characteristics

For

Flexron Syrup

(Ferric Ammonium Citrate + Folic acid + Cyanocobalamin

1. NAME OF MEDICINAL PRODUCT

Flexron syrup

2. QUALITATIVE AND QUANTITATIVE DESCRIPTION

Each 5ml of the syrup contains

Ferric Ammonium Citrate	200mg equivalent to 36mg elemental Iron
Folic acid	0.5mg
Cyanocobalamin	0.005mg

3. PHARMACEUTICAL FORM

Black coloured liquid oral preparation presented as sugar-based syrup and flavoured in 200ml amber PET bottle with dose measurement cap to facilitate easy dosing

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Flexron is an iron formulated product with vitamins. It is indicated for the treatment and prevention of nutritional deficiencies such as iron-deficiency, anaemia and folic acid deficiency in adults and in children.

4.2 Posology and method of administration

Posology

The safety and efficacy of all active pharmaceutical ingredients used in the formulation of Flexron syrup has been established in adults and paediatric populations when taken at the prescribed doses

Method of Administration

Age group	**Dose**
0-3yr	As directed by the physician
3-12yrs	5ml twice daily
12yrs and above	10mls twice daily

Or as directed by the physician.

4.3 Contraindications

Flexron is contraindicated in patients with iron metabolism disorder that causes increased iron storage like haemolytic anaemia, haemochromatosis, and haemosiderosis. It should not be use in anaemia not due to iron deficiency, and in case of renal failure

4.4 Special warnings and Precautions for Use

Long-term treatment

Long-term use of large doses may lead to iron overload. Patients with peptic ulcer and ulcerative colitis should use cautiously.

4.5 Drug Interactions

Antibiotics

Flexron decreases the absorption of some fluoroquinolones, tetracyclines and penicillamine derivatives, therefore doses should be separated by at least 3 hours.

Penicillamine and antituberculous drugs (such as isoniazid) may increase the requirements for folic acid

Neomycin used orally may reduce the absorption of vitamin B12.

Folic acid antagonists

Folate deficiency states may be produced by folic acid antagonists such as methotrexate, pyrimethamine, triamterene, trimethoprim and sulphonamides such as sulfasalazine.

Glucarpidase Folate deficiency states may be produced by glucarpidase

Oral contraceptives

Serum concentration of Vitamin B12 and folic acid may be decreased by use of oral contraceptives.

Antiepileptics

Folic acid has been reported to decrease serum concentrations of phenobarbital and phenytoin.

Antiepileptics may produce folate deficiency states.

Serum levels of anticonvulsant drugs may be reduced by the co-administration of folate e.g. folic acid possibly reduces the plasma concentration of phenobarbital, phenytoin and primidone.

Omeprazole

Omeprazole has been reported to impair the bioavailability of vitamin B12.

Raltitrexed

Concomitant use of folic acid with raltitrexed should be avoided.

Other

Absorption of vitamin B12 from the gastrointestinal tract may be reduced by aminosalicylic acid, histamine H2-antagonists, and colchicine.

4.6 Pregnancy and Lactation

Pregnancy

Active substances contained in Flexron have been found to be free of causing congenital malformations when administered during pregnancy. Rather, they have been found beneficial in preventing such malformations. Daily oral iron and folic acid supplementation with elemental iron and folic acid is recommended for pregnant women to prevent maternal anaemia, puerperal sepsis, low birth weight, and preterm birth. Even so, higher doses supplementation of elemental iron and folic acid is required in cases where a woman is diagnosed with anaemia during pregnancy

However, overdose of iron can cause miscarriage, birth defects or pregnancy-related diabetes. Although, what constitutes iron overdose may vary, as for most drugs the risk of toxicity is calculated on a mg/kg bodyweight basis.

Folic acid is helpful in furnishing new red blood cells. Folic acid preparations like Flexron yields a great advantage to fetus, as fetus can extract folate from maternal plasma, convert folate to a form that is not available for reverse transfer and use it for its own advantage.

Vitamin B12 is necessary for proper embryonic development and survival. It is necessary for baby's neural tube formation, brain and spine development. Changes in Vit B12 metabolism during pregnancy affect intestinal absorption, changes in plasma concentration and,

placental transport. An increase in Vit B12 intake, which Flexron furnishes, is needed to cover fetal storage

Lactation

Flexron is safe and beneficial for use in lactating mother.

4.7 Effects on ability to drive and use machine

Flexron has no influence on ability to drive and use machines

4.8 Undesirable effects

Ferric Ammonium Citrate

In high or toxic doses or poisoning- Gastrointestinal irritation, abdominal pain with nausea, vomiting and either diarrhoea or constipation, darkened stools, nausea and epigastric pain.

Long term or excessive administration may cause haemosiderosis.

Folic acid

Usually well tolerated, but may cause mild GI disturbances. Rarely, hypersensitivity reactions.

Vit B12

There are no known adverse effects in man.

4.9 Overdose

Iron poisoning from iron overdose has been reported which can be life-threatening. Acute iron poisoning in children can lead to bleeding, shock, acidosis and death.

If overdose occurs, patients should be monitored for evidence of toxicity and standard supportive treatment applied as necessary

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Pharmacotherapeutic group: Heamatinics

ATC code:

Mechanism of Action/Pharmacodynamics effects

Flexron contains active substances with synergistic, prophylactic and therapeutic actions, necessary for maintenance and/or improvement of functional activities of the body.

Iron compound and vitamins are included to treat deficiencies occurred. Anaemic conditions are characterized by low haem portion, which means low red cell functionality. Iron deficiency anaemia is characterized by a decrease in ferritin levels (normally 20-300mmol/l) which affects how iron is stored, a decrease in serum iron concentration (normally 10-30mmol/l), as well as decreased transferrin saturation of iron binding (normally 45-70mmol/l), which is how iron is transferred in the body. This causes the hematocrit and haemoglobin levels to fall very low (normal levels being 34.9%-50% and 12.0-17.5g/dl respectively). Iron therapy is initiated when haemoglobin levels falls below 13g/dl for men and less than 12g/dl for women. Generally, making 25mg of iron per day available will allow an iron deficiency anaemia to respond with a rise of 1% haemoglobin (0.15g/dl) per day and a reticulocyte response occurs between 4 and 12 days. An increase in the haemoglobin of at least 2g/dl after 3 weeks of therapy is a reasonable criterion of an adequate response. 5ml of Flexron contains about 200mg of Ferric ammonium citrate which is equivalent to 41mg of elemental iron

Ferric Ammonium Citrate

Ferric ammonium citrate is given as a supplement for iron release. Ferric ammonium citrate directly repairs haemoglobin deficiency by releasing about 16.5% to 18.5% elemental iron, which is absorbed in the upper layer of duodenum into the serum for haem synthesis. Ferric ammonium citrate, apart from releasing elemental iron, also inhibit hepcidin absorption thereby resulting in great pool of iron for haem synthesis. (Hepcidin is a hepatic protein that is known to inhibit iron release from macrophages and intestinal absorption of iron)

Folic acid

It is essential for erythropoiesis, maturation of red blood cells and biosynthesis of the DNA.

Vitamin B12 (Cyanocobalamin)

It is essential for erythropoiesis, formation of myelin sheet and synthesis of the DNA.

Clinical Efficacy and Safety

Ferric ammonium citrate is known to increase haemoglobin level through the release of elemental iron and inhibition of hepcidin.

5.2 Pharmacokinetics Properties

Iron (Ferric Ammonium Citrate)

Iron irregularly and incompletely absorbed from the gastrointestinal tract, the main sites of absorption being the duodenum and jejunum. Absorption is aided by the acid section of the stomach and by some dietary acids (such as ascorbic acid) and is more readily affected when the iron is in the ferrous state or is part of the haem complex (haem-iron). Absorption is also increased in conditions of iron deficiency or in the fasting state but is decreased if the body stores are overloaded. Only about 5 to 15% of the iron ingested in food is normally absorbed.

Most absorbed iron is bound to transferrin and transported to the bone marrow where it is incorporated into haemoglobin; the remainder is contained within the storage forms, ferritin or haemosiderin, or as myoglobin, with smaller amounts occurring in haem-containing enzymes or in plasma bound to transferrin. Only very small amounts of iron are excreted as the majority released after the destruction of the haemoglobin molecule is re-used.

Folic Acid

Folic acid is rapidly absorbed from the gastro-intestinal tract, mainly from the duodenum and jejunum. Folic acid administered therapeutically enters the portal circulation largely unchanged since it is a poor substrate for reduction by dihydrofolate reductase. It is converted to the metabolically active form 5-methyltetrahydrofolate in the plasma and liver. The principal storage site of folate is the liver; it is also actively concentrated in the CSF.

Folate undergoes enterohepatic circulation. Folate metabolites are eliminated in the urine and folate in excess of body requirements is excreted unchanged in the urine. Folate is distributed into breast milk. Folic acid is removed by haemodialysis.

Cyanocobalamin (Vit B12)

Cyanocobalamin bind to intrinsic factor, a glycoprotein secreted by the gastric mucosa, and are then actively absorbed from the gastro-intestinal tract. Absorption is impaired in patients with an absence of intrinsic factor, with a malabsorption syndrome or with disease or abnormality of the gut, or after gastrectomy. Absorption from the gastro-intestinal tract can also occur by passive diffusion. Cyanocobalamin is extensively bound to specific plasma proteins called transcobalamins; transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. Cyanocobalamin is stored in the liver, excreted in the bile and undergoes extensive enterohepatic recycling; part of an administered dose is excreted in the urine, most of it in the first 8 hours; urinary excretion, however, accounts for only a small fraction in the reduction of total body stores acquired by dietary means. Cyanocobalamin diffuses across the placenta and also appears in breast milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Sodium carboxyl methyl cellulose, Sucrose, Sodium methyl paraben, Sodium propyl paraben, Pineaple flavour.

6.2 Incompatibilities

Flexron should not be mixed with any other medicinal products, as compatibilities study has not been carried out

6.3 Shelf life

3 years

6.4 Special Precautions for Storage

Flexron should be stored in a cool dry place at temperatures not more than 30^{o}C

6.5 Nature and Contents of Container

Plain Amber-coloured Polyethylene terephthalates (PET) bottle with ROPP cap placed inside a paperboard carton

6.6 Special Precautions for disposal

Container and/or any unused product should be disposed in accordance with the local requirement

7. MANUFACTURER

BIOMEDICAL LTD
1, Ohimege Road, Industrial Estate
Ilorin Kwara State, PMB
1449