1. NAME OF THE MEDICINAL PRODUCT
Lady's Own Tonic

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 5ml contains:

Iron (as Ferrous Fumarate 30.95mg) 95.238mg
Thiamine Hydrochloride 1mg
Riboflavine 1mg
Pyridoxine Hydrochloride 5mg
Nicotinamide 15mg
Calcium D-Pantothenate 12mg
Cyanocobalamin 0.004mg
Zinc (as Zinc Sulphate) 4mg

For full list of excipients, see section 6.1.

3. Pharmaceutical form
Oral Syrup

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
- Dietary supplements of Vitamins and iron
- During pregnancy and lactation when there is increased Iron and vitamins requirements.
- Complaints of weakness due to blood loss from surgery, trauma and menstrual flows.
- During convalescence from debilitating illness.

4.2 Posology and method of administration
Posology

Adults: 10ml: 3 times daily
Children 7 – 12 years: 5ml 3 times daily

Method of administration

For oral administration.

4.3 Contraindications
- It is contra indicated in cases of known allergy to any of the ingredients, and in disturbances of iron metabolism. Lady's Own Tonic should not be taken by patients suffering from Stomach ulcers or other intestinal diseases.
- It is contra indicated in anaemias associated with ineffective erythropoiesis, bone marrow hypoplasia and sideroblastic change.
- In cases of idiopathic or secondary iron storage
- Anatacids reduce iron bioavailability and as such should not be administered concomitantly with haematinics. It should not be taken within one hour of administration of Antacids or Tetracyclines.

4.4 Special warnings and precautions for use
Use with caution in established cases of primary (idiopathic) or secondary iron storage and in anaemias associated with ineffective erythropoiesis.
All forms of iron therapy may cause temporary staining of the teeth and dark stools.

4.5 Interaction with other medicinal products and other forms of interaction
The Bioavailability of iron ingested with food is probably one half or one third of that seen in the fasting subject. Antacids also reduce the absorption of iron if given concurrently. Iron preparation may cause black discoloration of the stool, and sometimes darken the teeth with prolonged use.
It should not be taken within one hour of administration of Tetracycline.

4.6 Fertility, pregnancy and lactation

Pregnancy and Breastfeeding

No teratogenic effect has been reported with the use of Lady's Own Tonic in pregnant women however the normal rule that drugs should be avoided in the first trimester should be borne in mind.

4.7 Effects on ability to drive and use machines

Not relevant

4.8 Undesirable effects

Lady's Own Tonic is well tolerated. However as is typical of iron containing formulations, there could be occasional darkening of stools and manifestation of mild idiosyncratic reactions such as constipation, diarrhoea and vomiting. The occurrence of these is insignificant and as such negligible.

4.9 Overdose

Symptoms

Ingestion of 20 mg/kg elemental iron is potentially toxic and 200-250 mg/kg is potentially fatal. No single method of assessment is entirely satisfactory - clinical features as well as laboratory analysis must be taken into account. The serum iron taken at about 4 hours after ingestion is the best laboratory measure of severity.

Serum Iron	**Severity**
< 3 mg/L (55 micromol/L)	Mild toxicity
3-5 mg/L (55-90 micromol/L)	Moderate toxicity
> 5 mg/L (90 micromol/L)	Severe toxicity

Early signs and symptoms include nausea, vomiting, abdominal pain and diarrhoea. The vomit and stools may be grey or black.In mild cases early features improve but in more serious cases there may be evidence of hypoperfusion (cool peripheries and hypotension), metabolic acidosis and systemic toxicity. In serious cases, there can be recurrence of vomiting and gastrointestinal bleeding, 12 hours after ingestion. Shock can result from hypovolaemia or direct cardiotoxicity. Evidence of hepatocellular necrosis appears at this stage with jaundice, bleeding, hypoglycaemia, encephalopathy and positive anion gap metabolic acidosis. Poor tissue perfusion may lead to renal failure. Rarely, gastric scarring causing stricture or pyloric stenosis (alone or in combination) may lead to partial or complete bowel obstruction 2-5 weeks after ingestion.

Management

Supportive and symptomatic measures include ensuring a clear airway, monitor cardiac rhythm, BP and urine output, establishing IV access and administering sufficient fluids to ensure adequate hydration.
Consider whole bowel irrigation. If metabolic acidosis persists despite correction of hypoxia and adequate fluid resuscitation, an initial dose of 50 mmol sodium bicarbonate may be given and repeated as necessary, for adults guided by arterial blood gas monitoring (aim for a pH of 7.4). Consider the use of desferrioxamine, if /the patient is symptomatic (other than nausea), serum iron concentration is between 3-5 mg/L (55-90 micromol/L) and still rising. Haemodialysis does not remove iron effectively but should be considered on a supportive basis for acute renal failure as this will facilitate removal of the iron- desferrioxamine complex.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Iron bivalent, oral preparations

ATC code: B03AA02

Iron is an essential constituent of the body, and is necessary for haemoglobin formation and the oxidative processes of living tissues. Iron and iron salts should be given for the treatment or prophylaxis of iron deficiency anaemias. Preparations of iron are administered by mouth, by intramuscular or intravenous injection.

Soluble ferrous salts are most effective by mouth. Ferrous fumarate is an easily absorbed source of iron for replacement therapy. It is a salt of ferrous iron with an organic acid and is less irritant to the gastro-intestinal tract than salts with inorganic acids.

Lady's Own Tonic is an iron, and vitamins formulation. It contains Iron in the stable, absorbable ferrous state and also some other important erythropoietic factors such as vitamins B_{12}. Lady's Own Tonic also contains calcium which enhances bone and teeth development. Most enzymes function better, metabolic activities are enhanced and overall health is improved.

Iron

Iron is an essential constituent of the body, being necessary for haemoglobin formation and for the oxidative process of living tissues. The body contains about 4g of iron most of which is present as haemoglobin. The remainder is present in the storage forms, ferritin or haemosiderin, in the reticuloendothetial system or as myoglobin with smaller amount occurring in haem-containing enzymes or in plasma bound to tranferrin.
Iron and iron salts should only be given for the treatment of other types of anaemia except where iron deficiency is also present. Iron deficiency anaemia should be determined and treated.
Compound of iron are used in the treatment of microcytic anaemia, including simple achlorhydric anaemia, simple anaemia of pregnancy, the nutritional anaemia of infants, anaemia due to excessive haemorhage and anaemia associated with infections and malignant disease.
Externally, some iron salts are powerfully astringent and stypic. Iron therapy should be continued after the haemoglobin concentration has returned to normal, to replenish the body stores of iron.

Vitamin B_1 (Thiamine)

Thiamine is practically devoid of pharmacodynamic actions when given in usual therapeutic doses; even large doses produce no discernible effects. Isolated clinical reports of toxic reaction to the long-term parenteral administration of Thiamine probably represent rare instances of hypersensitivity.
The only established therapeutic use of Thiamine is in the treatment or the prophylaxis of Thiamine deficiency. The syndromes of Thiamine deficiency seen clinically can range from beriberi through wernicke's encephalopathy and korsakoff's syndrome to alcoholic polyneuropathy. Thiamine, a water-soluble vitamin, is an essential coenzyme for carbohydrate metabolism. Thiamine deficiency develops when the dietary intake is inadequate; severe deficiency leads to chronic beriberi characterized by peripheral neuritis, bradycardia, muscle weakness and paralysis.

Vitamin B_2 (Riboflavin)

Riboflavine, a water-soluble vitamin, is essential for the utilization of energy from food. The active, phosphorylated forms, flavine mononucleotide and flavine adenine dinucleotide are involved as coenzymes in oxidative/reductive metabolic reactions.
Riboflavine deficiency develops when the dietary intake is inadequate. Deficiency leads to the development of a well-defined syndrome known as ariboflavinosis, characterized by cheilosis, angular stomatitis, glossitis and seborrhoeic keratosis of the nose and ano-genital region. There may be ocular symptoms including itching and burning of the eyes, photophobia and corneal vascularisation. Riboflavine deficiency may occur in association with other vitamin B complex deficiency states such as pellagra.
Riboflavine is used in the treatment and prevention of Riboflavine deficiency.

Vitamin B_6 (Pyridoxine)

Pyridoxine, a water–soluble vitamin is involved principally in amino acid metabolism, but is also involved in carbohydrate and fat metabolism. It is also required for the formation of haemoglobin.

Deficiency of Pyridoxine is rare in humans due to its wide spread distribution in foods. Pyridoxine deficiency may however be drug induced and can occur, for instance, during isoniazid therapy. Inadequate Pyridoxine deficiency in adults lead to the development of peripheral neuritis, deficiency in children also affect the CNS. Pyridoxine is used in the treatment and prevention of Pyridoxine deficiency states. Pyridoxine has also been used to treat seizure due to hereditary syndromes of Pyridoxine deficiency or dependency in infants.
Pyridoxine has also been tried in a wide variety of other disorders, including the treatment of depression and other symptoms associated with the premenstrual syndrome and the use of oral contraceptives.

Nicotinamide

Nicotinic acid and nicotinamide, the form that occurs naturally in the body are water-soluble vitamin B substances, which are converted to Nicotinanide Adenine Dinucleotide Phosphate (NADP). These coenzymes are involved in electron transfer reactions in the respiratory chain.
Nicotinamide deficiency develops when dietary intake is inadequate. Deficiency leads to the development of a syndrome known as pellagra characterized by skin lesions, especially on areas exposed to sunlight, with hyperpigmentation and hyperkeratinisation. Other symptoms include diarrhoea, abdominal pain, glossitis,

stomatitis, and loss of appetite, headache, lethargy and mental and neurological disturbances. Nicotinic acid deficiency may occur in association with other vitamin B complex deficiency states.
Nicotinamide is used in the treatment and prevention of Nicotinic acid deficiency. Nicotinamide is preferred, as it does not cause vasodilatation.

Calcium D-Pantothenate
Pantothenic acid is traditionally considered to be a vitamin B substance. It is a component of co-enzyme A which is essential in the metabolism of carbohydrate, fat and protein.
Deficiency of pantothenic acid is unlikely in man because of its wide spread distribution in food. It is administered as a nutritional supplement often as calcium salt and usually in conjunction with other vitamins of the B group.

Vitamin B_{12} (Cyanocobalamin)
Vitamin B_{12}, water-soluble vitamins occur in the body mainly as methylcobalamin and as adenosylcobalamin and hydroxycobalamin. It act as coenzyme in nucleic acid synthesis.
Vitamin B_{12} deficiency may occur in strict vegetarians with an inadequate dietary intake, in patients with malabsorption syndromes or metabolic disorder, nitrous oxide induced megaloblastosis or following anaemias and neurological damage.
Vitamin B_{12} preparations are used in the treatment and prevention of Vitamin B_{12} deficiency. It is desirable to identify the cause of deficiency before commencing therapy. Treatment usually results in rapid haematological improvement and a striking clinical response.

Zinc
Zinc is an essential part element of nutrition and traces are present in a wide range of foods. Zinc is an integral part of at least 70 metalloenzymes including carbonic anhydrase, lactic dehydrogenase, alkaline phosphatase, carboxypeptidase, aminopeptidase and alcoholic dehydrogenase.
It is also a co-factor in the synthesis of DNA and RNA, and it is involved in the mobilization of vitamin A from the liver and in the enhancement of follicle-stimulating hormone and leuteinising hormone. It is essential for normal cellular immune functions and for spermatogenesis and normal testicular function, and it is important in the stabilization of membrane structure.
Zinc salts are used as supplements
to correct zinc deficiency.

5.2 Pharmacokinetic properties

Iron
Iron is irregularly and incompletely absorbed from the gastro-intestinal tract the main sites of absorption being the duodenum and jejunum. Absorption is usually increased in conditions of iron deficiency or when given in the fasting state. Absorption of iron may be reduced in certain disease states.
Apart from haemorhage, iron is mainly lost from the body in the faeces, urine, skin and sweat, but the total loss is small. In healthy men and non-menstruating women the loss is replaced by the absorption of about 1mg of iron daily; about 2mg needs to be absorbed daily by menstruating women.
In childhood and adolescence, the need is proportionately greater because of growth. In pregnancy and lactation 3mg or more must be absorbed daily.

Vitamin B_1 (Thiamine)
Thiamine is well absorbed from the gastro intestinal tract following oral administration, although the absorption of large doses is limited. It is also rapidly absorbed following intra muscular administration. It is widely distributed to most body tissues and appears in breast milk. Thiamine is not stored to any appreciable extent in the body and amounts in excess of the body's requirements are excreted in the urine as unchanged Thiamine or as metabolites.
Thiamine requirements are directly related to the carbohydrate intake and the metabolic rate. A daily dietary intake of 1 to 1.3mg of Thiamine is recommended for healthy men and 0.7 to 1mg for healthy women.

Vitamin B_2 (Riboflavin)
Riboflavine is readily absorbed from the gastro intestinal tract. Although Riboflavine is widely distributed to body tissues, little is stored in the body. Riboflavine is converted in the body to the coenzyme Flavine mononucleotide and then to another coenzyme Flavine adenine dinucleotide. About 60% of FMN and FAD are bound to plasma proteins. Riboflavine is excreted in urine, mainly as metabolites. As the dose increases, larger amounts are excreted unchanged. Riboflavine crosses the placenta and is distributed in breast milk.
The Riboflavine requirement is often related to the energy intake but it appears to be more closely related to the resting metabolic requirements. A daily dietary intake of about 1.3 to 1.8mg of Riboflavine is recommended.

Vitamin B_6 (Pyridoxine)
Pyridoxine is readily absorbed from the gastro-intestinal tract following oral administration and is converted to the active forms pyridoxal phosphate and pyridoxamine phosphate. They are stored mainly in the liver where there is oxidation to 4-pyridoxic acid, which is excreted in the urine. Pyridoxine crosses the placenta and also appears in the breast milk.
For adults, the daily requirement of Pyridoxine is probably about 2mg and this amount is present in most normal diets. Meats, especially liver, cereals, eggs, fish and certain vegetables and fruits are good source of Pyridoxine.

Nicotinamide
Nicotinamide is absorbed readily from all portions of the intestinal tract and the vitamin is distributed to all tissues. The principal route of metabolism of Nicotinic acid and nicotinamide is by the formation of N—methylnicotinamide, which in turn is metabolized further. Smmall amounts of the unchanged vitamins appear in the urine following therapeutic doses of nicotinic acid and nicotinamide.The daily adult requirement is probably about 15-20mg.

Calcium D-Pantothenate
Pantothenic acid is readily absorbed from the gastro intestinal tract following oral administration. It is widely distributed in the body tissues and appears in breast milk. About 70% of Pantothetic acid is excreted unchanged in the urine and about 30% in the fences.

Pantothenic acid is rapidly absorbed in foods-meat, legumes and whole grain cereals are particularly rich sources. Recommended daily intakes of Pantothenic acid have not been set, but human requirements are adequately met by a daily intake of about 4 to 10mg.

Vitamin B_{12} (Cyanocobalamin)
Vitamin $\mathbf{B_{12}}$ substances bind to intrinsic factor 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.
Vitamin $\mathbf{B_{12}}$ is extensively bound to specific plasma proteins called Transcobalamins, Transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. It is stored in the liver, excreted in the bile and undergoes enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours. Vitamin $\mathbf{B_{12}}$ diffuses across the placenta and also appears in breast milk.
For adults, the daily requirement of Vitamin $\mathbf{B_{12}}$ is probably about 1 to 3µg and this amount is present in most normal diets.

Zinc
Zinc and its salts are poorly absorbed from the gastrointestinal tract; only a small portion of dietary zinc is absorbed. Zinc is distributed widely in the body and is primarily excreted in the faeces with only traces appearing in the urine since the kidneys have little or no role in regulating the content of zinc in the body.

5.3 Preclinical safety data
No further data.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Aspartame
Methyl Hydroxybenzoate
Propyl Hydroxybenzoate
Citric Acid
Sorbitol Solution (70%)
Caramel
Ascorbic Acid
Xanthan Gum
Polysorbate 80
Deionised Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years

6.4 Special precautions for storage

Store below 30°C. Protect from light.

6.5 Nature and contents of container

200ml Amber bottle with aluminium screw cap.

6.6 Special precautions for disposal and other handling

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

7. APPLICANT/MANUFACTURER

SKG-Pharma Limited
7/9 Sapara Street,
Ikeja, Lagos State, Nigeria.
Tel: +234(1)44544640
Email: skg-pharma@yahoo.com