

**1. NAME OF THE MEDICINAL PRODUCT**

HAEPLER® BLOOD TONIC

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each 5ml contains Iron and Vit. B- Complex

(For a full list of excipients, see section 6.1).

**3. PHARMACEUTICAL FORM**

Liquid- Tonic

**4. Clinical particulars**

**4.1 Therapeutic indications**

**Vitamin B1 (Thiamine Mononitrate)**

Thiamine is essential CO enzyme for carbohydrate metabolism. Severe deficiency leads to the development of a syndrome know as beri-beri

**Vitamin B2 (Riboflavine)**

Riboflavine is essential for the utilization of energy from food. Deficiency leas to the development of driboflavinosis. Characterized by Cheilosis, angular stomatitis, glossitis, keratitis and seborrheic dermatitis.

**Vitamin B6 (Pyridoxine)**

Pyridoxine is involved principally in amino acid metabolism, but is also involved in carbohydrate and fat metabolism.

It is required for the formation of hemoglobin.

Pyridoxine is used in the treatment of depression and other symptoms associated with the premenstrual syndrome and use of oral contraceptives.

**Vitamin B12 (Cyanocobalamin)**

- 1) Used in the treatment and prevention of megaloblastic anemias and neurological damage.
- 2) Used in the treatment of megaloblastosis caused by prolonged nitrous oxide anaesthesia which inactivates the vitamin, and in the rare syndrome of congenital transcobalamin deficiency.

**Folic Acid**

Used in the treatment of megaloblastic and macrocytic anemias due to folate deficiency; dietary supplement to prevent neural tube defects.

**Iron (from Ferric ammonium citrate)**

Iron supplement are indicated in the prevention and treatment of iron deficiency anemia which may result from inadequate diet, malabsorption, pregnancy, rapid growth during childhood and or blood loss.

### **Nicotinamide**

Used to prevent and treat nicotinic acid deficiency (pellagra)

In Summary

Haepler blood Tonic is a supplement for prevention of Vitamin deficiency in conditions such as galactosaemia, disaccharide intolerance, Phenyl ketonuria and other disorders of carbohydrate or amino acid metabolism, as well as in patient who are on restricted, specialized or synthetic diet.

Haepler blood Tonic is indicated for the treatment of iron deficiency where there is an associated deficient intake or increased need for B-Complex Vitamins.

## **4.2 Posology and method of administration**

Haepler blood Tonic is administered Orally

Dosage

Adult: 10ml one to three times daily

Children: 5ml one to three times daily

Haepler blood Tonic should be taken with or immediately after meal.

## **4.3 Contraindications**

Hypersensitivity to any ingredient of the formulation.

Haemosiderosis, haemochromatosis and patient with hereditary optic nerve atrophy.

## **4.4 Special warnings and precautions for use**

Haepler Blood Tonic is well tolerated at recommended doses. However as is typical of Iron containing formulation there could be darkening of stool, diarrhoea, constipation and vomiting or nausea. The gastro-intestinal irritations can be reduced and controlled by taking blood tonic with or immediately after meals

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

## **4.6 Pregnancy and Lactation**

In controlled Studies with women, vitamin preparation in Haepler at the usual dosage during the course of the first trimester resulted in no fetal risks. There are no signs indicating a risk , if this type of preparation is taken during the second and third trimesters, the probability of injuring the fetus appears to be very low. Folic acid crosses the placenta. However, adequate and well controlled studies in humans have not shown that folic acid caused adverse effects on the Fetus.

Problems in humans have not been documented with intake of normal daily recommended amounts of Iron.

#### **4.7 Effects on ability to drive and use machines**

No influence on the ability to drive or use machines

#### **4.8 Undesirable effects**

Long term or excessive administration may cause haemosiderosis, peripheral vascular thrombosis and epigastric pain

Hydralazine and Isoniazid may decrease the effect of pyridoxine.

Pyridoxine may decrease the effect of Levodopa. Folic acid may decrease response to methotrexate.

Folic may lower, serum phenytoin concentrations, phenytoin may lower serum folate concentration.

#### **4.9 Overdose**

Large overdoses of water-soluble vitamins are readily excreted in the urine. No emergency procedure or antidote is applicable and any symptoms are rapidly reduced upon withdrawal of the preparation.

Initial symptoms of the iron overdose include nausea, vomiting, diarrhoea, abdominal pain, haematemesis, rectal bleeding, lethargy and circulatory collapse. Hyperglycaemia and metabolic acidosis may also occur.

Treatment

- To minimize or prevent further absorption of the medication, as follows  
Induce vomiting e.g. by administration of an emetic
- Gastric lavage with desferrioxamine Solution (2g/L). Then desferrioxamine (5-10g in 50-100ml of water) should be introduced into the stomach to be retained.
- Severe poisoning: shock and/or come with high iron levels (serum iron > 90 micromol/L in Children, > 142 micromol/L in adults); immediate supportive measures plus i.v. infusion of desferrioxamine should be instituted.
- Less severe poisoning; i.v. desferrioxamine is recommended (1g 4-hourly in Children; 50mg/kg to a maximum dose of 4g in adults).

## **5. PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamics properties**

Pharmacotherapeutics group: Hematinic syrup, ATC code: B03AE01

**Ferric Ammonium Citrate:** Ferric Ammonium Citrate is one of the best-tolerated iron supplements. It rapidly supplements elemental iron so that iron deficiency is quickly controlled, thus leading to faster correction of anaemia and replenishment of tissue iron stores.

Each 5ml of Haepler® Blood Tonic provides 69mg of Ferric Ammonium Citrate that is equivalent to 14 mg of elemental iron. Thus, when an adult takes the recommended dosage of 1 tablespoonful twice a day, he gets 28 mg of elemental iron which is sufficient amount of elemental iron per day for an adult patient suffering from mild to moderate iron deficiency.

**Folic Acid:** It is so called because it is present in green leaves, which is chemically pteroylglutamic acid. It is a growth promoter. It helps in the synthesis of Deoxyribose Nucleic Acid (DNA), the building block of life. It is essential for proper maturation of red cells. It helps in inter conversion and metabolism of amino acids.

**Cyanocobalamin:** Cyanocobalamin (Vitamin B12) is a complex organo-metallic compound in which a cobalt atom is placed within a corrin ring. It plays an important role in synthesis of DNA and maturation of red cells. It acts as a co-enzyme in certain steps necessary for genetic replication.

## **5.2 Pharmacokinetic 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:** 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.

### **5.3 Preclinical safety data**

#### Toxicology

**Iron:** Iron is a general cellular poison and is directly corrosive to the GI mucosa. Cellular toxicity The absorption of excessive quantities of ingested iron results in systemic iron toxicity. Severe overdose causes impaired oxidative phosphorylation and mitochondrial dysfunction, which can result in cellular death. The liver is one of the organs most affected by iron toxicity, but other organs such as the heart, kidneys, lungs, and the hematologic systems also may be impaired.

**MILD TO MODERATE POISONING:** Vomiting and diarrhea may occur within 6 hours of ingestion.

**SEVERE POISONING:** Severe vomiting and diarrhea, lethargy, metabolic acidosis, shock, GI hemorrhage, coma, seizures, hepatotoxicity, and late onset GI strictures.

**Folic acid:** The risk of toxicity from folic acid is low, because folate is a water-

soluble vitamin and is regularly removed from the body through urine. One potential issue associated with high dosages of folic acid is that it has a masking effect on the diagnosis of pernicious anaemia (vitamin B12 deficiency).

Vitamin B12:

Vitamin B12 is usually considered a non-toxic substance. Even taking it by injection at high doses does not seem to increase the risk for toxicity

## **6.0 PHARMACEUTICAL PARTICULARS**

### **6.1 List of Excipients**

Sucrose (Dry Sugar)  
Xanthan Gum  
Methyl Paraben  
Propyl Paraben  
Citric Acid  
Ethanol 96%  
Caramel Concentrate (Flavor)  
Raspberry Essence (Liquid)  
Vanilla Flavor (Liquid)  
Purified Water  
Sodium Hydroxide (pH Adjustment)

### **6.2 Incompatibilities**

None known

### **6.3 Shelf life**

24 Months

### **6.4 Special precautions for storage**

Store below 30°C in tight container Protect from light and moisture.

### **6.5 Nature and contents of container and special equipment for use, administration or implantation**

Haepler® - Blood Tonic is available in Amber 200ml Plastic bottle.

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

No special requirements.

**7 APPLICANT/MANUFACTURER**

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