SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

TONIFER syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Ferric ammonium citrate…… ……. ……200.0 mg
(equivalent to 40 mg of elemental iron)
Folic acid…… 0.5 mg
Vitamin B12……5.0 mcg
Per 5 ml

Excipients with known effects : sucrose, sodium methylparaben, sodium propylparaben , sorbitol.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Syrup oral

4. CLININCAL PARTICULARS

4.1. Therapeutic indications

TONIFER syrup is indicated for :

- Iron deficiency anaemia due to chronic blood loss, hookworm infestation, inadequate dietary iron intake, etc.
- Dimorphic anaemia due to combined deficiency of iron, folic acid and/or vitamin B12.
- Anaemia associated with pregnancy and lactation.
- General weakness, loss of appetite, debilitated states, and convalescence.
- Post surgical states and other debilitating conditions.
- Post surgical infections.

4.2. Posology and method of administration

Posology

As recommended by a physician.

Posology recommendation (5 ml of syrup contains 40 mg of iron (Fe)):
Curative treatment:
Adults and children > 30 kg: 100 to 200 mg of iron per day, divided into 2 doses.
Children 20-30 kg : 100 to 150 mg Iron by day, split into 2 sockets.
Children < 20 kg: Adjust the dose according to weight: 3 to 6 mg of iron/kg/day, divided into 2 sockets.
Preventive treatment :
Adult: 60 mg of iron by day gone in 2 doses.

Take between meals.

Do not exceed the prescribed dose.

Method of administration

Oral route

4.3. Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.

- Patients suffering hypervitaminosis.
- Patients suffering from pernicious anemia
- Contraindicated at the house of THE patients reached of porphyria cutaneous late,of hemochromatosis, of hemosiderosis , of anemia hemolytic anemia and anemia due to bone marrow failure.

4.4. Special warnings and precautions for use

General

Do not exceed the recommended dose. The type of anemia, the underlying cause or causes must be determined before starting treatment with this medication. Anemia may be the result of a systemic disturbance such as recurrent blood loss, the cause or the causes underlying must be corrected, if possible.

Salts of iron

In general, people with a history of kidney disease, bowel disease, disease of the ulcer gastroduodenal, enteritis, colitis, pancreatitis, hepatitis, who consume alcohol in excessive quantities, who are planning to become pregnant, or who are over 55 years old and have in the Family members with a history of heart disease should consult a doctor. and a pharmacist Before of take of iron.

People suffering from blood disorders and requiring frequent blood transfusions are also at risk of iron overload and do not should not take iron supplements without the advice of a healthcare professional. Long-term use of high doses of iron may cause hemosiderosis , which clinically resembles hemochromatosis. Iron overload is associated with several genetic diseases, including hemochromatosis. The accumulation of excess iron East studied For determine if it is of a contributor potential of the diseases neuro- degenerative such that there disease Alzheimer's And there disease Parkinson's.

Acid folic

An untreated vitamin B12 deficiency that has been progressing for more than 3 months can produce has of the permanent degenerative lesions of there bone marrow spinal cord.

Folic acid at doses above 0.1 mg per day can mask pernicious anemia because a remission haematological can se produce SO that THE demonstrations neurological progress. This can lead to serious damage to the nervous system before a [condition] is established. Correct diagnosis. Neurological manifestations will not be prevented by folic acid, and If they are not treated with vitamin B12, irreversible damage will occur. doses suitable of vitamin B12 can prevent, Stop, Or improve THE changes neurological caused by anemia pernicious.

Administering folic acid alone is an inappropriate therapy for pernicious anemia and other megaloblastic anemias in which vitamin B12 is deficient. The doses of Cyanocobalamin doses above 10 mcg per day may produce a hematological response in Patients with folate deficiency. Inappropriate administration may mask a diagnosis correct.

Caution is advised with patients undergoing angioplasty because an intravenous loading dosefolic acid, vitamin B6 and vitamin B12, followed by daily oral administration After coronary stent placement, the rate of restenosis could increase. Because of this risk potentially, this vitamin combination should not be prescribed for patients receiving stents coronary arteries.

Vitamin B 12

Multivitamins are not recommended for the treatment of severe specific deficiencies in vitamins and minerals. In such cases, the underlying cause must be determined and corrected if It's possible. Multivitamins are not intended for the treatment of pernicious anemia, because... involvement neurological can se develop or progress despite there remission temporary of anemia in patients with vitamin B12 deficiency who receive folic acid additional And Who are insufficiently treated with there vitamin B12.

4.5. Interactions with other medicinal products and other forms of interaction

Salts of iron

- The effectiveness of iron is reduced when iron salts and the following products are ingested: aluminum hydroxide, aluminum phosphate, calcium, aluminum carbonate (basic), the chloramphenicol, dihydroxyaluminium aminoacetate , carbonate dihydroxyaluminium of sodium, magaldrate , carbonate of magnesium, hydroxide of magnesium, oxide of magnesium, trisilicate of magnesium, methacycline , minocycline , oxytetracycline , rolitetracycline And bicarbonate of sodium.

- The effectiveness of the molecules is reduced in the case of absorption of iron salts and molecules following: cefdinir , cinoxacin , ciprofloxacin enoxacin , gatifloxacin , gemifloxacin , grepafloxacin , levofloxacin , lomefloxacin , moxifloxacin , norfloxacin , ofloxacin penicillamine sparfloxacin , temafloxacin , mesylate of trovafloxacin And levothyroxine.

- The effectiveness of iron and molecules is reduced in the case of absorption of iron salts and of the products following: zinc (with decrease of absorption gastrointestinal), acid acetohydroxamic acid , trientine (with decrease) of gastrointestinal absorption).

- Iron absorption and bioavailability are reduced when iron salts are ingested and the following products: esomeprazole, desferrioxamine , gossypol , lansoprazole, omeprazole, pantoprazole, rabeprazole, soy, soy protein, vanadium, cholestyramine, colestipol and pancrelipase .

- Absorption of the molecules East diminished in case absorption of iron And of the molecules The following: Ciprofloxacin, ofloxacin, levofloxacin , tiludronate , risedronate , alendronate , etidronate , ibandronate , levodopa, methyldopa , levothyroxine, acid mycophenolic , minocycline , doxycycline, tetracycline and demeclocycline .

- Allopurinol can increase iron storage in the liver and should not be used in combination with supplements iron.

- Aminosalicylic acid can cause malabsorption syndrome (weight loss, depletion of iron And of vitamin, steatorrhea).

- Aspirin and NSAIDs can cause damage to the mucous membranes and bleeding in the entire gastrointestinal tract. chronic blood loss associated with the use of long-term effects of these agents may contribute to Iron deficiency anemia. Iron supplements Because they can also irritate the gastrointestinal tract, patients should not use them. in even time that THE NSAID less that that is recommended by a doctor.

- Chloramphenicol can reduce there effect to the therapy of iron in anemia iron-deprived.

- Iron supplements and dimercaprol can combine in the body to form a product harmful chemical.

- Adequate dietary iron intake is recommended when taking H2 blockers such as cimetidine, ranitidine, famotidine, or nizatidine. Iron supplements are generally not necessary unless used for another indication.

Acid folic

- The effectiveness of folate is reduced when folic acid is taken with the following: fosphenytoin, phenytoin, and pyrimethamine.
- Folate absorption is reduced when folate is taken with the following: aminosalicylic acid, antacids, antibiotics, aspirin, carbamazepine, cholestyramine, colestipol, cycloserine, cimetidine, famotidine, nizatidine, ranitidine, pancrelipase, sulfasalazine, and triamterene.
- Serum folate levels are reduced when the following are taken: conjugated estrogens, oral contraceptives, methotrexate, methylprednisolone sodium succinate (noted in individuals with multiple sclerosis), intravenous pentamidine, phenobarbital, primidone, and pyrimethamine.
- Excessive alcohol consumption increases the need for folic acid.
- Chloramphenicol can antagonize some of the effects of folic acid on the blood (hematopoietic system). Limited data suggest that diuretics may increase folic acid excretion.
- Reduced vitamin B12 and, to a lesser extent, folate levels occur in some people with diabetes and may contribute to hyperhomocysteinemia, adding to the already elevated risk of cardiovascular disease. The reduced folate levels seen in diabetics have been linked to metformin use in some cases, possibly due to reduced folic acid absorption. Symptomatic folate deficiency is unlikely to occur with metformin, but people with diabetes may need folic acid supplements to reduce hyperhomocysteinemia.
- Chronic smoking is associated with decreased folate levels.
- Folate-dependent enzymes have been inhibited in laboratory experiments by ibuprofen, naproxen, indomethacin, and sulindac.
- One study found that administering folic acid to pregnant women may not interfere with the protective effect of the sulfadoxine-pyrimethamine combination when used for intermittent preventive treatment of malaria.

- There is a common belief that folic/folinic acid supplements do not interfere with the therapeutic effects of trimethoprim. However, this view has been challenged, and failure of trimethoprim therapy has rarely occurred when folinic acid has been administered concurrently.

4.6. Pregnancy and breastfeeding

Nutritional supplements of vitamins and minerals are generally considered to be safe during pregnancy.

Salts of iron

Pregnancy category B

The use of iron supplements during pregnancy is considered a recommendationaccepted and safe, benefiting both mother and child. Due to negative interactions of iron affects the intestinal absorption of other divalent minerals; therefore, supplemental iron doses shouldto be as low as possible while still fulfilling their purpose. It is not known whether iron salts pass through the placenta.

Fetal malformations were less common in women who had taken iron during the pregnancy compared to those who did not take it. In addition, the group of women who took iron hasdelivered infants with a higher birth weight and there were fewer cases of births premature.

Acid folic

Pregnancy category A
Folic acid requirements increase significantly during pregnancy, and deficiency can harm the fetus. Folic acid is recommended for women planning a pregnancy or who are pregnant to prevent birth defects caused by folic acid deficiency. Folic acid crosses the placenta.
Studies in pregnant women have not shown that folic acid increases the risk of fetal abnormalities when administered during pregnancy. If the drug is used during pregnancy, the possibility of harming the fetus appears to be ruled out. However, because studies cannot exclude the possibility of harm, folic acid should only be used during pregnancy if clearly needed.
All women who could become pregnant are advised to consume folate to reduce the risk of neural tube defects in the fetus. Taking a higher dose of folic acid than recommended is classified as FDA Pregnancy Category C.

Vitamin B 12

No problems have been identified in humans when taking normal recommended daily doses.

Breastfeeding

Salts of iron

The available evidence and/or expert consensus are inconclusive or insufficient to determine the risk to the baby when the medication is used during breastfeeding. The potential benefits of drug treatment must be weighed against the potential risks before the medication is prescribed during breastfeeding.

Acid folic

Folic acid is excreted in human breast milk. During breastfeeding, folic acid requirements are significantly increased; however, the amounts in breast milk are sufficient to meet infants' needs, although supplementation may be necessary for low birth weight infants, those breastfed by mothers with folic acid deficiency, or those suffering from prolonged diarrheal infections. Use of the medication during breastfeeding, under the supervision of a healthcare professional, is likely safe. Adverse effects in breastfed infants related to normal daily folic acid intake during breastfeeding have not been observed. The potential benefits of drug therapy should be weighed against the potential risks before the medication is prescribed during breastfeeding.

Vitamin B12

No breastfeeding problems have been observed in humans when taking normal recommended daily doses.

4.7. Effects on aptitude to drive of the vehicles And has to use of the machines

Without object

4.8. Undersirable effects

Iron salts

Side effects of iron therapy may include constipation, diarrhea, nausea, vomiting, dark stools, and abdominal pain. These side effects are usually temporary. Gastrointestinal disturbances, including nausea, vomiting, constipation, diarrhea, and dark stools, have been observed. Gastrointestinal side effects are relatively common, and increasing dietary fiber or taking over-the-counter medications may be recommended to manage these side effects.

Folic acid

Folate appears to be well tolerated at recommended doses. Cases of stomatitis, alopecia, myelosuppression, and zinc depletion have been reported.

Cases of erythema, urticaria, skin redness, rash, itching, nausea, bloating, flatulence, cramps, bitter taste, and diarrhea have been reported. Urine color may increase.

Cases of irritability, excitability, general malaise, changes in sleep patterns, vivid dreaming, hyperactivity, confusion, impaired judgment, increased seizure frequency, and psychotic behavior have been reported.

Very high doses may cause significant central nervous system side effects. Folic acid supplementation may increase seizures in individuals with epileptic disorders, particularly at very high doses. Folic acid can mask the symptoms of pernicious, aplastic, or normocytic anemias caused by vitamin B12 deficiency and may lead to neurological damage.

Cases of anaphylaxis and bronchospasm have been reported.

Vitamin B 12

Vitamin B12 is generally well tolerated by the body. Occasionally, reactions may occur, but these disappear quickly after continuous and regular use.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals should report any suspected adverse reactions using the FRILAB reporting form available under the pharmacovigilance tab of the website: www.frilab.ch

4.9. Overdose

Iron salts

The clinical course of acute iron overdose can be variable. Early symptoms may include abdominal pain, nausea, vomiting, diarrhea, loose stools, melena, hematemesis, hypotension, tachycardia, metabolic acidosis, hyperglycemia, dehydration, drowsiness, pallor, cyanosis, fatigue, seizures, shock, and coma.

Symptoms of acute iron overdose or accumulation may include arthritis, signs of gonadal insufficiency (amenorrhea, early menopause, loss of libido, impotence), and shortness of breath/dyspnea. High doses can cause vomiting and diarrhea, followed by cardiovascular or metabolic toxicity and death. It is unknown whether elevated levels are associated with cancer, coronary artery disease, or myocardial infarction (MI or heart attack).

Folic acid

Except during pregnancy and breastfeeding, folic acid should not be administered at therapeutic doses exceeding 0.4 mg daily until pernicious anemia has been ruled out. Patients with pernicious anemia receiving more than 0.4 mg of folic acid daily who are inadequately treated with vitamin B12 may show a return of hematological parameters to normal, but the neurological manifestations due to vitamin B12 deficiency will progress. Doses of folic acid exceeding the RDA should not be included in multivitamin preparations; if therapeutic amounts are required, folic acid should be given separately.

Vitamin B 12

No specific information on vitamin B12 overdose is available.

5. PHARMACOLOGICAL PROPERTIES

5.1. Properties pharmacodynamics

Pharmacotherapeutic class : IRON PREPARATIONS code ATC : B03AE01 (B: Blood and hematopoietic organs)

Iron salts

Iron salts are compounds used primarily for the prevention and treatment of iron deficiency anemia. The body stores iron in compounds called ferritin and hemosiderin because it is essential for the formation of hemoglobin. Sufficient amounts of iron are necessary for efficient erythropoiesis. Iron also serves as a cofactor for several essential enzymes, including cytochromes, which are all involved in electron transport. Iron absorption varies depending on the body's existing iron stores, the form and amount of iron in food, and the combination of foods in the diet. The inorganic ferrous form of iron is more readily absorbed.

Folic acid

Folic acid is necessary for the synthesis of nucleoproteins, purine nucleotides, and the metabolism of certain amino acids; normal cell growth and reproduction; normal nucleoprotein synthesis; and the maintenance of normal erythropoiesis.

It is converted in the liver and plasma into its metabolically active form, tetrahydrofolic acid, by dihydrofolate reductase, which then acts as a one-carbon acceptor. These acceptors are attached at several different positions to form six major congeners, each of which plays a specific role in intracellular metabolism. Coenzymes formed from folic acid play a crucial role in the following intracellular metabolic processes: conversion of homocysteine to methionine, conversion of serine to glycine, thymidylate synthesis, histidine metabolism, purine synthesis, and the utilization or production of formate.

Methylenetetrahydrofolate is a methyl donor in the conversion of homocysteine to methionine. This reaction requires vitamin B12 as a cofactor. Individuals with alanine substituted for valine in the gene for methylenetetrahydrofolate reductase have elevated homocysteine levels and an increased risk of coronary heart disease.

Tetrahydrofolate aids in the conversion of serine to glycine by accepting a methylene group from serine. Pyridoxal phosphate is required as a cofactor. The resulting product, 5,10-methylenetetrahydrofolic acid, is an essential coenzyme in thymidylate synthesis. In this reaction, a methyl group is donated to deoxyuridylic acid to form thymidylic acid. This step limits the rate of DNA synthesis. Megaloblastic changes resulting from folic acid deficiency are secondary to the failure of thymidylate synthesis.

Tetrahydrofolate also acts as a formimino group acceptor for histidine, forming tetrahydrofolic formimino and glutamic acid. Two steps in purine nucleotide synthesis require folic acid derivatives. These derivatives, 5,10-methenyltetrahydrofolate and 10-formyltetrahydrofolate, donate carbon atoms to the growing purine ring. The utilization or production of formate is assisted by tetrahydrofolate and 10-formyltetrahydrofolate.

Vitamin B_{12} (Cyanocobalamin)

Vitamin B12 is present in the body primarily as methylcobalamin, adenosylcobalamin, and hydroxocobalamin. These act as coenzymes in the transmethylation of homocysteine to methionine; in the isomerization of the coenzyme methylmalonyl to succinyl coenzyme; and with folic acid in several metabolic pathways, respectively. Vitamin B12 deficiency interferes with hematopoiesis and results in megaloblastic anemia.

5.2. Properties pharmacokinetics

Iron

Absorption

In iron deficiency anemia, the initial response to orally administered iron takes one week. Hemoglobin levels may increase by 1.5 to 2.2 g/dL/week for the first two weeks, then by 0.7 to 1.6 g/dL/week until normal hemoglobin levels are reached. Reticulocyte counts increase within 3 to 4 days and reach their peak after 7 to 10 days.

When administered orally, subjects with normal iron stores absorb 10–35%; iron-deficient patients absorb 80–95%. The percentage of absorption is affected by the salt form, the amount administered, the dosing regimen, and the size of iron stores. Orally administered iron is poorly absorbed by patients undergoing continuous peritoneal dialysis. Vitamin C promotes the absorption of non-heme iron. Ferrous iron is more bioavailable than ferric iron.

The absorption of a pharmacological dose of iron was assessed by determining mucosal absorption, mucosal transfer, and retention of 33 mg of Fe(II) as ferrous sulfate and ferrous ascorbate in 11 subjects with normal iron stores and 9 subjects with iron deficiency. No difference in absorption was observed between the two iron compounds in normal subjects. In contrast, the absorption of ferrous ascorbate was on average 52% higher than that of ferrous sulfate in

subjects with iron deficiency. This difference was due to greater mucosal absorption, likely because the oxidation of Fe(II) in the alkaline environment of the intestine, which leads to the formation of non-absorbable Fe(III), was prevented.

For comparison, all current studies concern 40% absorption of the reference dose of ferrous ascorbate, as this corresponds to that which is obtained at the limit in populations deficient in borderline iron.

Effects of food

The main dietary enhancers of non-heme iron absorption are muscle tissue (cysteine-containing proteins) and ascorbic acid. The main dietary inhibitors of non-heme iron absorption are phytic acid, polyphenols, calcium, and certain proteins.

Elimination
The elimination half-life of the parent compound is 6 hours. Excretion occurs in trace amounts in the kidneys and feces.

Folic acid

The therapeutic drug concentration of folic acid in a healthy adult ranges from 4 to 20 ng/mL. It appears in the plasma approximately 15 to 30 minutes after taking an oral dose; the peak concentration is usually reached within 60 to 90 minutes.

Absorption

The bioavailability of folic acid ranges from 76% to 93%. Folic acid is absorbed primarily in the proximal small intestine via a mediated transport process. Absorption is minimal in the distal jejunum and virtually nonexistent in the distal ileum. Absorption is reported to be impaired in the proximal jejunum of patients with celiac disease, but absorption in the distal jejunum is comparable to that of healthy individuals. Pregnancy does not appear to impair folic acid absorption.

Distribution

Folate derivatives are bound by plasma proteins. The highest affinity for plasma protein binding occurs with unmethylated analogs. Other distribution sites include the liver (50%) and tissues. Once absorbed, folic acid and its derivatives are rapidly distributed throughout the body's tissues. Normal serum, cerebrospinal fluid, and erythrocyte folate levels indicate the following measurements, respectively: 5–15 ng/mL; 16–21 ng/mL; and 0.175–0.316 mcg/mL. In general, serum folate levels below 5 ng/mL indicate folate deficiency, and levels below 2 ng/mL typically result in megaloblastic anemia.

Metabolism

Folic acid is metabolized in the liver to 7,8-dihydrofolic acid and, eventually, to 5,6,7,8-tetrahydrofolic acid, with the help of a reduced diphosphopyridine nucleotide (DPNH) and folic acid reductases. This conversion occurs primarily in the liver; during absorption across the intestinal mucosa, the conversion does not occur to a significant extent. Tetrahydrofolic acid derivatives are distributed to all tissues of the body but are stored mainly in the liver.

Excretion

The kidneys excrete 30% of folic acid. After a single oral dose of 100 micrograms of folic acid in a limited number of healthy adults, only a minimal amount of the drug appears in the urine. The other route of excretion is the bile. After oral administration, folic acid is found in concentrations ranging from 15 to 400 ng/mL in the bile, with peak levels occurring approximately 120 minutes after absorption. Small amounts of orally administered folic acid have been recovered in the feces. Folic acid is also excreted in the breast milk of nursing mothers.

Vitamin B_{12} (Cyanocobalamin)
Cyanocobalamin is absorbed from the gastrointestinal tract and is highly bound to specific plasma proteins. A study with labeled vitamin B12 showed that it was rapidly taken up by the intestinal mucosa and remained there for 2–3 hours. Peak concentrations in blood and tissues do not occur until 8–12 hours after absorption, and peak concentrations are found in the liver within 24 hours. Cobalamins are stored in the liver, excreted in the bile, and undergo enterohepatic recycling. A portion of the dose is excreted in the urine, mostly within the first 8 hours.

5.3. Preclinical safety data

Without object

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sorbitol 70%, sucrose, sodium methylparaben , sodium propylparaben , sodium hydroxide, citric acid monohydrate, disodium EDTA, caramel flavour, Fantop orange oil flavour , Bronopol , sodium saccharin, menthol, sodium citrate.

6.2. Incompatibilities

Without object

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at a temperature below 30°C and away from light.

6.5. Nature and contents of container

Bottle made of PET 200 ml with small measure

6.6. Special precautions for disposal and handling

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

7. HOLDER, OPERATORS AND MANUFACTURERS

Holder and operator of the marketing authorization
FRILAB ITS
17, rue des Pierres du Niton1207
Geneva SWITZERLAND

Manufacturer
Athena Drug Delivery Solutions Pvt. Ltd.
Made by
Sanpras Healthcare Pvt . Ltd.
At: Plot No.- 81, STICE, Musalgaon , Tal. Sinnar, District Nashik, 422 112 Maharashtra State, India

8. DATE OF REVISION OF THE TEXT

10 October 2025

9. DOSIMETRY

Without object.

CONDITIONS FOR PRESCRIPTION AND DISPENSING

This medication is not subject to medical prescription.