SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product: I-UP TABLETS

(Ferrous Ascorbate & Folic Acid Tablets)

2. QUALITATIVE AND QUANTITATIVES COMPOSITION:

Each film coated tablet contains:

Ferrous Ascorbate equivalent To Elemental Iron……. 100 mg

Folic Acid BP …… 1.5 mg

Excipients……. ……q.s

Colour : Ferric Oxide Red USP-NF (Red Oxide of Iron)

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Film coated tablet

Visualdescriptionoffinishedproduct: Brick Red colour capsule shaped biconvex film coated tablets.

4. Clinical particulars:

4.1 Therapeutic indications:

Indicated in the treatment of iron deficiency anemia, menorrhagia and folate deficiency anemia.

Ferrous ascorbate reduces the risk of pre-eclampsia (pregnancy-induced hypertension) which generally occurs in severe or very severe anemia. Folic acid can reduce the risk of fetal neural tube defects.

4.2Dosage and Method of Administration

1 tablet daily or as directed by the physician.

4.3 Contraindications

Hypersensitivity to iron, should be avoided in patients who have bacterial infections. Contraindicated in patients who have hemosiderosis, hemochromatosis, and hemolytic anemia.

4.4 Warnings

Oral iron may aggravate existing peptic ulcer, regional enteritis and ulcerative colitis.

4.5 Drug Interactions

Absorption of iron is inhibited by magnesium trisilicate and antacids containing carbonates. Since oral iron products interfere with absorption of oral tetracycline antibiotics, these products should not be taken within two hours of each other. Iron absorption may also be inhibited by the ingestion of milk or eggs.

4.6 Pregnancy and lactation

For the prevention and treatment of iron deficiency and to supply a maintenance dosage of folic acid.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Side Effects

Nausea, regurgitation, constipation, pyrosis (burning sensation in the chest), upset stomach may occur with the use of hematinic.

Iron may cause your stools to turn black, an effect that is not harmful.

4.9 Overdosage

Overdose occurs only rarely in adults but can occur in children. Toxicity due to an excessive intake is caused by iron overdosage. Initial symptoms result from the contact irritation of iron on gastrointestinal mucosa: nausea, vomiting, diarrhoea, epigastric pain, hematemesis and rectorrhages. The situation may progress and late complications are hypotension, coma, hepatocellular necrosis and renal impairment. To decrease absorption, gastric lavaging with sodium bicarbonate 1% and monitoring of the patient are recommended. In adults a solution of manitol or sorbitol may be used to stimulate the intestinal emptying. Deferoxamine (mesylate) is a chelating agent that binds ferric ions to the groups 3-hydroxamic of the

molecule, being effective when administered early in the treatment of acute intoxication. Intubation and hemodynamic therapy maybe required in more severe situations.

5. Pharmacological Particulars

5.1 Pharmacodynamic properties

Ferrous Ascorbate (Iron):

Iron salts are compounds used primarily for the prophylaxis and treatment of iron deficiency anaemia. The body stores iron in compounds called ferritin and hemosiderin since it is an essential component in the formation of haemoglobin. Adequate amounts of iron are necessary for effective erythropoiesis. Iron also serves as a cofactor of several essential enzymes, including cytochromes, all of which are involved in electron transport. Iron absorption is a variable of the existing body iron stores, the form and quantity in foods, and the combination of foods in the diet. The ferrous form of inorganic iron is more readily absorbed.

Folic Acid

Folic acid is required for synthesis of nucleoprotein, purine nucleotides and the metabolism of some amino acids, normal growth and cell reproduction, nucleoprotein synthesis and the maintenance of normal erythropoiesis.

It is converted in the liver and plasma to its metabolically active form, tetrahydrofolic acid, by dihydrofolate reductase, which then acts as an acceptor of one-carbon units. These are attached at several different positions to form six major congeners, each of which plays a specific role in intracellular metabolism. The coenzymes formed from folic acid are instrumental in the following intracellular metabolisms: Conversion of homocysteine to methionine, conversion of serine to glycine, synthesis of thymidylate, histidine metabolism, synthesis of purines, and the utilization or generation of formate.

Methyltetrahydrofolate is a methyl donor in the conversion of homocysteine to methionine. This reaction requires vitamin B12 as a cofactor. Individuals with an alanine to valine substitution in the gene for 5,10- methylenetetrahydrofolate reductase have elevated homocysteine and an elevated risk for coronary artery disease.

Tetrahydrofolate assists 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-methylenetetrahydrofolate, is an essential coenzyme in the synthesis of thymidylate. In this reaction, a methyl group is donated to deoxyuridylic acid to form thymidylic acid. This is a rate-limiting step in DNA synthesis. The megaloblastic changes produced by folic acid deficiency are secondary to the failure of thymidylate synthesis.

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

5.2 Pharmacokinetics

Ferrous Ascorbate (Iron)

Absorption: In case of iron-deficiency anaemia, the initial response of iron given orally is 1 week. Haemoglobin may increase 1.5 to 2.2 g/dl/week for the first 2 weeks and then 0.7 to 1.6 g/dl/week until normal haemoglobin levels are achieved. Reticulocyte count increases in 3 to 4 days and peaks in 7 to 10 days.

Given orally, subjects with normal iron stores absorb 10 - 35%; iron-deficient patients absorb 80 - 95%. The percent absorption is affected by the salt form, the amount administered, the dosing regimen, and the size of the iron stores. Oral iron is poorly absorbed by patients on continuous peritoneal dialysis. Vitamin C enhances absorption of non-haem iron. Ferrous iron is more bioavailable than ferric iron.

The absorption of a pharmacological dose of iron was assessed by determination of mucosal uptake, mucosal transfer and retention of 33 mg Fe (II) as ferrous sulphate and ferrous ascorbate in 11 subjects with normal iron stores and 9 subjects with iron deficiency. There was no difference in absorption between the two iron compounds in normal subjects. Absorption of ferrous ascorbate averaged 52% higher than ferrous sulphate in subjects with iron deficiency. The difference was the result of higher mucosal uptake, probably because the oxidation of Fe (II) in the alkaline milieu of the intestine, which leads to formation of non-absorbable Fe (III) complexes, was prevented.

For purposes of comparison, all studies currently refer to 40% absorption of the reference dose of ferrous ascorbate since it corresponds to that which is obtained in borderline iron-deficient populations.

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

Elimination: The elimination half-life of the parent compound is 6 hours. Excretion takes place in trace amounts through the kidneys and the faeces.

Folic acid

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

Absorption: The bioavailability of folic acid ranges from 76% to 93%. Folic acid is absorbed by a carrier-mediated process primarily in the proximal part of the small intestine. There is little absorption in the distal jejunum and practically none in the distal ileum. Its absorption is reported to be impaired in patients with celiac disease in the proximal jejunum, but absorption is reported to be comparable to that for healthy individuals from the distal jejunum. Pregnancy does not appear to impair the absorption of folic acid.

Distribution: Folate derivatives are bound by plasma proteins. The greatest affinity for plasma protein-binding occurs with the non-methylated analogs. Other distribution sites include the liver (50%) and tissues. Once absorbed, folate and its derivatives are rapidly distributed to all body tissues. Normal serum, cerebrospinal fluid and erythrocyte levels of folate have been reported to be 5 - 15 ng/mL; 16 - 21 ng/mL and 0.175 - 0.316 mcg/mL, respectively. In general, folate serum levels below 5 ng/mL indicate folate deficiency, and levels below 2 ng/mL usually result in megaloblastic anaemia.

Metabolism: Folic acid is metabolized in the liver to 7,8-dihydrofolic acid and, eventually, to 5,6,7,8-tetrahydrofolic acid with the aid of a reduced diphosphopyridine nucleotide (DPNH) and folate reductases. This conversion occurs primarily in the liver and not to any significant degree during absorption through the intestinal mucosa. Tetrahydrofolic acid derivatives are distributed to all body tissues but are stored primarily in the liver.

Excretion: The kidneys excrete 30% of folic acid. After a single oral dose of 100 mcg of folic acid in a limited number of normal adults, only a trace amount of the drug appeared in the urine. The other route of excretion is bile. Following oral administration, folic acid is found in concentrations ranging from 15 - 400 ng/mL in the bile, with peak levels occurring in approximately 120 minutes. Small amounts of orally administered folic acid have also been recovered in the faeces. Folic acid is also excreted in the milk of lactating mothers.

6. Pharmaceutical particulars

6.1 List of excipients

Microcrystalline cellulose pH 102

Sodium starch Glycollate (Type A)

Aerosil – 200

Talcum Powder

Magnesium Stearate

Sodium Lauryl Sulphate

Crospovidone

Hydroxy Propyl Methyl Cellulose E-5

Polyethylene Glycol-6000

Talcum Powder

Isopropyl Alcohol (Isoproponol)*

Methylene Chloride*

Ethyl cellulose

Titanium Dioxide

Iron red oxide

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

24 months.

6.4 Storage:

Store in a dry place, below 30° C. Protect from light.

Keep out of reach of children.

6.5 Nature and contents of container

Alu–Alu Blister Pack of 10 Tabletsand such 3 Blisters packed in a printed monocartonalong with pack insert.

6.6 Special precautions for disposal and other handling

Not Applicable

7. Marketing authorization holder

Cachet Pharmaceuticals Pvt. Ltd.

Address:415, Shah Nahar, Worli,

Mumbai 400 018. India.

Phone No. Office +91-22-40829991

Email: - regulatory@cachetpharma.com

8. Marketing authorization number(s)

07187/08146/NMR/2020

9. Date of first authorization/renewal of the authorization

10/03/2022

10. Date of revision of the text

01/07/2023