PROFESSIONAL INFORMATION

FERRITONE

Complementary Medicine: Health Supplement

This unregistered medicine has not been evaluated by the SAHPRA for its quality, safety or intended use.

SCHEDULING STATUS: S0

1. NAME OF THE MEDICINE

FERRITONE powder

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 g sachet contains:

Liposomal ferric pyrophosphate	307 mg
Equivalent to ferric pyrophosphate	80 mg
Providing iron (elemental)	24 mg
Magnesium L-ascorbate dihydrate	118 mg
Providing ascorbic acid (vitamin C)	100 mg
and magnesium (elemental)	6.5 mg
L-5-methyltetrahydrofolate	385 µg
Providing folic acid	200 µg
Methylcobalamin	2,5 mg
Providing cobalamin (vitamin B12)	5 µg

Sugar free.

Contains sweetener: 5 mg stevia per sachet.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Powder

Off-white powder with vanilla flavour.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

FERRITONE is a health supplement that provides iron, vitamin C, folic acid, and vitamin B12 (cobalamin). It contributes to the normal formation and proper function of red blood cells and haemoglobin.

4.2. Posology and method of administration

Posology

Adults and children 1 year and older

The usual dose is 1 sachet per day. Sachets should be reconstituted in ± 100 ml of water or juice. After reconstitution, FERRITONE is a cloudy, slightly sweet suspension with a distinct vanilla taste. Once opened, sachets should be used immediately.

Quinolone or tetracycline antibiotics, bisphosphonates, and certain other medicines should be taken at least 2 hours before or 4 to 6 hours after FERRITONE (see section 4.5).

Patients can continue with FERRITONE supplementation for as long as they derive benefit from it.

Method of administration

For oral administration.

See section 4.5 for instructions on how to take FERRITONE in combination with other medicines.

See section 6.6 for reconstitution instructions.

If possible, FERRITONE should be taken on an empty stomach to prevent possible binding of iron by calcium, polyphenols, tannins, or other dietary constituents in the gut. While this liposomal iron formulation enhances gastrointestinal availability and tolerability, people who are unable to tolerate taking FERRITONE on an empty stomach should be advised to avoid taking it at the same time as dairy, coffee, tea, or cereals.

4.3. Contraindications

FERRITONE is contraindicated in:

- Patients with hypersensitivity to any of the components of the formulation (see section 2, section 4,4 and section 6.1)
- Iron overload (including haemochromatosis).

4.4. Special warnings and precautions for use

FERRITONE provides vitamin B12 that contains cobalamin and cobalt that may cause allergic reactions in people with hypersensitivity to these compounds (see section 4.3).

Since achlorhydria may impair iron absorption, patients with this condition might not derive benefit from oral iron supplementation with FERRITONE.

Iron supplementation is associated with an increased risk of nosebleeds in patients with hereditary haemorrhagic telangiectasia. Caution is required. Advise patients to discontinue use if they experience an increase in frequency of nosebleeds.

FERRITONE contains folic acid and vitamin B12, which, in combination with vitamin B6, have been associated with an increased rate of restenosis after placement of bare metal coronary stents. Patients with coronary stents should use FERRITONE only under the supervision of their cardiologist.

FERRITONE contains 200 µg folic acid per recommended daily dose. This amount is not considered sufficient to influence seizure frequency in people with seizure disorders as doses of less than 1 mg of folic acid have rarely been associated with increased seizure activity. Advise patients with seizure disorders to adhere to the maximum recommended dose (see section 4.2).

It is not known whether supplementation with vitamin C benefits the growth of cancer cells or whether it may reduce the effects of chemotherapy. Cancer patients should use FERRITONE only under the supervision of their oncologist (see section 4.5).

Vitamin C (ascorbic acid) is metabolised to oxalic acid. High doses of vitamin C may increase the risk of developing oxalate urinary stones, especially in people prone to

oxalate nephrolithiasis. Increased consumption of ascorbic acid increases the amount of oxalic acid excreted in the urine. Those with a history of oxalate kidney stones seem to be more sensitive to supplementation with vitamin C and reports have shown that supplemental vitamin C 1 gram per day can increase stone risk by 40 % in this patient group. In men, daily supplemental vitamin C in doses of 250 mg have also been associated with a higher risk of nephrolithiasis. Adult patients who are prone to develop kidney stones should be advised to strictly adhere to the recommended maximum daily dosage which provides 200 mg of vitamin C (see section 4.2). Additional care is required in patients with chronic kidney disease, as the risk for nephrolithiasis may be even higher.

Patients, especially children, with glucose-6-phosphate dehydrogenase (G6PD) deficiency should use FERRITONE with caution and should strictly adhere to the recommended maximum daily dose (see section 4.2) as they may be at risk of developing acute haemolytic anaemia if vitamin C is taken in high doses.

4.5. Interactions with other medicines and other forms of interaction

Interaction with Medicines

ALUMINIUM COMPOUNDS

The vitamin C in FERRITONE may increase the amount of aluminium absorbed from aluminium compounds. In individuals with normal renal function, it is likely that urinary excretion of aluminium increases, making aluminium retention and toxicity unlikely. However, patients with renal failure who chronically take aluminium-containing

compounds, such as phosphate binders, should strictly adhere to the recommended maximum daily dose of 1 sachet (see section 4.2).

BISPHOSPHONATES

It is not known to what extent the liposomal ferric pyrophosphate in FERRITONE might reduce absorption of bisphosphonates through the formation of insoluble complexes in the gut. Advise patients to separate doses of bisphosphonates by at least two hours from doses of all other medicines, including supplements such as FERRITONE.

CHEMOTHERAPY

Patients receiving chemotherapy should use FERRITONE only under the supervision of their oncologist given the vitamin C and folic acid in the formulation (see section 4.3).

INTEGRASE INHIBITORS

It is not known to what extent the liposomal ferric pyrophosphate in FERRITONE might reduce the absorption of integrase inhibitors (e.g., dolutegravir, raltegravir). If FERRITONE and integrase inhibitors are taken concurrently, bloods levels and pharmacodynamic effects of these antiretrovirals may be reduced. To avoid this interaction, advise patients to take dolutegravir at least 2 hours before or 6 hours after FERRITONE.

LEVODOPA

Studies in healthy people suggest that that iron forms chelates with levodopa, thus reducing the amount of levodopa absorbed with about 50 %. The clinical significance of this has not been determined. It is advised that patients separate doses of levodopa and FERRITONE by as much as possible.

LEVOTHYROXINE

It is not known to what extent the liposomal ferric pyrophosphate in FERRITONE might reduce absorption of levothyroxine (due to the formation of insoluble complexes in the gut). Advise patients to separate levothyroxine and FERRITONE doses by at least two hours.

METHOTREXATE

There is some evidence that supplementation with folic acid may reduce the efficacy of methotrexate in the treatment of acute lymphoblastic leukaemia and possibly other cancers. Advise cancer patients to discuss supplementation with FERRITONE with their oncologist. In patients who receive long-term, low-dose methotrexate for rheumatoid arthritis or psoriasis, supplementation with folic acid may reduce the incidence of side effects without reducing efficacy.

METHYLDOPA

It is not known to what extent the liposomal ferric pyrophosphate in FERRITONE might decrease methyldopa concentrations by reducing its absorption through chelation. The

clinical impact on blood pressure has not been determined. Advise patients to separate doses of methyldopa and FERRITONE by at least 2 hours.

MYCOPHENOLATE MOFETIL

It is not known to what extent the liposomal ferric pyrophosphate in FERRITONE might decrease mycophenolate mofetil absorption, if at all. If concurrent therapy is considered necessary, advise patients to take FERRITONE four to six hours before, or two hours after, mycophenolate mofetil.

ESTROGENS

There have been reports of increases in plasma levels of estrogen of up to 55 % when vitamin C was taken concurrently with oral contraceptives or hormone replacement therapy, including topical products. It has been postulated that vitamin C prevents tissue oxidation of estrogen, regenerates oxidised estrogen, and reduces sulphate conjugation of estrogen in the gastrointestinal wall. With high tissue levels of vitamin C, these processes are already maximised, and supplemental vitamin C does not have any effect on plasma estrogen levels. Increases in plasma estrogen levels may arise when women who are deficient in vitamin C, take supplements, such as FERRITONE. Monitor such patients for estrogen-related side effects.

PENICILLAMINE

It is not known whether the liposomal ferric pyrophosphate in FERRITONE will reduce the absorption of penicillamine. Advise patients to separate doses by at least 2 hours.

PHENYTOIN AND OTHER ANTI-EPILEPTIC MEDICINES

Although only reported for high doses (1 mg daily or more), supplemental folic acid may exacerbate seizures in people with seizure disorders. Doses less than 1 mg, as in FERRITONE, have rarely been associated with increased seizure activity. However, it is nevertheless advised that patients on phenobarbital and primidone should be monitored for increased seizure activity following initiation of supplementation with FERRITONE.

In addition, folic acid may be a cofactor in phenytoin metabolism. Although only reported for doses of 1 mg per day or more, folic acid may reduce serum levels of phenytoin in some patients. It is recommended that serum phenytoin levels are monitored at the onset and with cessation of supplementation.

PYRIMETHAMINE

The folic acid in FERRITONE may antagonise the antiparasitic effect of pyrimethamine against toxoplasmosis and *Pneumocystis carinii* pneumonia. Since malaria parasites cannot utilise exogenous folic acid, this interaction is not relevant when pyrimethamine is administered for the treatment of malaria.

QUINOLONE AND TETRACYCLINE ANTIBIOTICS

Iron may decrease the absorption of quinolone and tetracycline antibiotics due to formation of insoluble complexes in the gastrointestinal tract. It is not known to what extent this interaction occurs with the use of liposomal ferric pyrophosphate. Advise patients to take quinolone antibiotics at least 2 hours before or 2 hours after

FERRITONE. Similarly, patients should take FERRITONE at least 2 hours before or 4 hours after tetracycline antibiotics.

WARFARIN

Vitamin C in high doses may reduce the response to warfarin, possibly by causing diarrhoea and reducing warfarin absorption. While lower doses may be safe, patients may still require regular monitoring of their INR (International Normalised Ratio) especially when supplementation with FERRITONE is initiated or discontinued.

Interactions with herbs and supplements

ACEROLA AND ROSE HIP

Caution is advised when FERRITONE is combined with herbs such as acerola and rose hip that contain high concentrations of vitamin C. Concomitant use of acerola and rose hip with FERRITONE might exceed the tolerable upper intake level (UL) of 2000 mg vitamin C per day for adults and this could increase the risk of developing side effects.

CHROMIUM

It is possible that the vitamin C in FERRITONE may increase chromium absorption. The amount of chromium absorbed after a 1000 µg dose approximately doubled when vitamin C 100 mg was given at the same time. Advise people to avoid taking large doses of chromium and FERRITONE together. It is not known whether this interaction can be avoided by separating the doses by several hours.

GRAPE SEED POLYPHENOLS

There is preliminary evidence that patients with hypertension who took both vitamin C 500 mg/day plus grape seed polyphenols 1000 mg/day had significantly increased systolic and diastolic blood pressure. The potential mechanism of this interaction is not known. Advise patients to exercise caution when combining FERRITONE with grape seed polyphenols and to strictly adhere to the recommended maximum daily dosage.

Interactions with laboratory investigations

The extent to which the liposomal ferric pyrophosphate in FERRITONE may interfere with guaiac tests for occult faecal blood is unclear. Beware of possible false-positive results.

The vitamin C in FERRITONE may potentially interfere with several laboratory tests, including blood assays for acetaminophen, aspartate aminotransferase, bilirubin, carbamazepine, creatinine, lactic dehydrogenase (LDH), and theophylline. It may also interfere with tests for occult blood.

Vitamin B12 in FERRITONE can cause a false-positive test result for intrinsic factor antibodies.

Advise people taking FERRITONE to inform their doctor, pharmacist, or nurse that they are taking supplemental iron and vitamin C when scheduled for special investigations.

4.6. Fertility, pregnancy, and lactation

Pregnancy

FERRITONE is considered safe in pregnancy when used orally and appropriately. Care must be exercised when FERRITONE is combined with other supplements that contain iron, vitamin C, folic acid, and vitamin B12 to ensure that the upper tolerable intake levels (UL) of these supplements are not exceeded.

Lactation

FERRITONE is considered safe while breastfeeding when used orally and appropriately. Advise breastfeeding women to adhere to the dosage instructions above.

Fertility

The effects of FERRITONE on male and female fertility are not known.

4.7. Effects on ability to drive and use machines

No studies on the effect on the ability to drive and to use machines have been performed. Given its side-effect profile, it is unlikely that FERRITONE will influence the ability to drive or operate machinery. However, it is not always possible to predict how patients may react to FERRITONE. Patients should be advised to determine how it affects them before they engage in these activities.

4.8. Undesirable effects

a. Summary of safety profile

Iron is generally well tolerated with the most common side effects being gastrointestinal in nature, such as abdominal pain, constipation, diarrhoea, gastrointestinal irritation, nausea, and vomiting. Liposomal formulations have been shown to improve gastrointestinal tolerability.

Supplemental vitamin C is generally well tolerated. Adverse effects associated with oral supplementation with vitamin C are dose-related and are more likely to occur at doses above the tolerable upper intake level (UL) of 2000 mg per day in adults. Such adverse effects may include abdominal cramps, esophagitis, heartburn, headache, osmotic diarrhoea, nausea, and vomiting.

Folic acid is generally well tolerated in supplemental doses less than 1 mg daily. FERRITIONE provides 200 µg of folic acid per daily dose and thus the amount of folic acid in the formulation is unlikely to produce the cardiovascular, gastrointestinal, and dermatological adverse events seen with doses of between 1 to 15 mg per day.

Vitamin B12 is generally well tolerated when taken orally.

b. Tabulated summary of adverse reactions

There are no data available on adverse reactions for the combination. Below is a summary of adverse events for iron (non-liposomal formulations), vitamin C, folic acid, and vitamin B12 reported individually:

IRON

Gastrointestinal disorders

Less frequent: Dry mouth, gastrointestinal irritation, heartburn, abdominal pain, constipation, diarrhoea, nausea, vomiting (uncommon in doses below 45 mg of elemental iron per day), oral or gastric ulcerations, discolouration of teeth

VITAMIN C

Nervous system disorders

*Frequency unknown**: Fatigue, headache, insomnia, and sleepiness (dose-related)

(* Cannot be estimated from available data)

Vascular disorders

Frequency unknown: Thickening of the carotid arterial wall when used in high doses (see section 4.8c below)

Gastrointestinal disorders

Frequent: Nausea, vomiting, esophagitis, heartburn, abdominal cramps, gastrointestinal obstruction, diarrhoea

Renal and urinary disorders

Frequency unknown: Nephrolithiasis, haematuria, hyperoxaluria, hyperuricosuria, crystalluria (see section 4.4)

FOLIC ACID

Immune system disorders

Frequency unknown: Allergic reactions (e.g., bronchospasm and anaphylactic shock)

VITAMIN B12

Immune system disorders

Frequency unknown: Allergic reactions, including rash, pruritus, erythema, urticaria

Skin and subcutaneous tissue disorders

Frequency unknown: Acneiform eruptions

c. Description of selected adverse reactions

Large amounts of vitamin C have been associated with an increased rate of carotid inner wall thickening in men (500 mg vitamin C daily), increased risk of mortality in postmenopausal women with diabetes (doses greater than 300 mg daily) as well as the precipitation of oxalate renal stones. FERRITONE contains 200 mg vitamin C

(ascorbic acid) per recommended daily dose. This dosage is not known to affect such adverse events to a clinically relevant extent.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions is important. It allows continued monitoring of the benefit/risk balance of FERRITONE. Healthcare providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on the SAHPRA website.

In addition, adverse events can also be reported to Flora Force Health Products (Pty) Ltd via email at info@floraforce.co.za or telephonically [0861 336723].

4.9. Overdose

Acute iron overdosage, 60 mg/kg and more, can cause vomiting, haematemesis, and diarrhoea, followed by cardiovascular, liver, or metabolic toxicity, and death. In pregnant women, iron overdose (with peak levels > 400 µg/dl) have been associated with organ failure, spontaneous abortion, preterm delivery, and maternal death. Iron exerts its toxic effects from its corrosive action in the gastrointestinal tract and from the presence of unbound iron in the serum. Circulating, free iron produces vasodilation that may give rise to hypotension and shock.

Long-term use of high doses of iron can cause hemosiderosis that clinically resembles haemochromatosis.

Treatment of iron overdose

Paediatric and adult patients with known ingestion of 40 mg/kg or greater of elemental iron or those with severe or persistent symptoms related to iron ingestion must be referred to a healthcare facility for medical evaluation. Gastric lavage should only be considered if the patient presents within 1 to 2 hours of ingestion.

Whole bowel irrigation may be considered if a significant quantity remains in the bowel after lavage, but caution is required in any patient who may have sustained mucosal damage. Contraindications to whole bowel irrigation include major gastrointestinal dysfunction, such as ileus, bowel obstruction, perforation, or significant gastrointestinal haemorrhage.

Determine haemoglobin, haematocrit, white cell count, blood glucose, electrolytes, acid-base status, and blood typing. Take blood for determination of iron concentration 4 to 6 hours post-ingestion and repeat after 2 to 4 hours. After 12 hours of ingestion, iron would have been redistributed to the tissues and serum iron concentrations are of little clinical value.

Shock and acidosis should be appropriately managed with careful attention to fluid balance to avoid pulmonary oedema.

Patients with iron levels < 54 µmol/l (< 300 µg/dl) or who remains asymptomatic 6 hours after ingestion of the overdose are not expected to develop significant toxicity and do not require active treatment. Patients with iron levels of 54 – 90 µmol/l (300 to 500 µg/dl) must be observed for symptoms of iron toxicity.

Intravenous deferoxamine should be administered irrespective of symptoms if iron concentration is > 90 µmol/l (> 500 µg/dl). Clinical indications for deferoxamine are

moderate to severe systemic toxicity, such as cardiovascular shock, gastrointestinal bleeding, lethargy and central nervous system depression, metabolic acidosis, and iron-induced hepatotoxicity. Deferoxamine should NOT be used in patients who display only direct gastrointestinal toxicity.

Cessation of metabolic acidosis and resolution of systemic toxicity are considered reasonable endpoints of chelation therapy.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Category: Complementary Medicine

Class: D34.12 Health Supplement: Multiple Substance Formulation

Iron contributes to the reduction of tiredness and fatigue, helps to form red blood cells and haemoglobin, and helps in their proper function, contributes to normal cognitive function, helps to maintain immune function, and is a factor in the maintenance of good health. Bodily iron occurs mostly as part of haemoglobin in erythrocytes and myoglobin in myocytes where it is utilised for oxygen and carbon dioxide transport. Iron also functions as an electron carrier in the electron transport chain in cytochromes. It is also present in the functional groups of the majority of enzymes in the Krebs cycle. Iron is an essential cofactor in the synthesis of neurotransmitters such as dopamine, noradrenaline (norepinephrine), and serotonin.

Vitamin C partakes in various physiological functions including tyrosine metabolism, and acts as cofactor in the synthesis of carnitine, thyroxin, noradrenaline

(norepinephrine), dopamine, and tryptophan. It is furthermore involved in a variety of metabolic processes. These include oxidation-reduction reactions and cellular respiration, synthesis of lipids and proteins, carbohydrate metabolism, catabolism of cholesterol to bile acids, conversion of folic acid to folinic acid, and iron metabolism. It also acts as an antioxidant and helps to maintain proper immune function. It is also important for optimal iron absorption.

Folic acid helps to form red blood cells and contributes to maternal tissue growth during pregnancy. If taken daily prior to becoming pregnant and during early pregnancy, it helps to reduce the risk of neural tube defects.

Vitamin B12 contributes to normal erythropoiesis, to a reduction of tiredness and fatigue, and to the normal functioning of the immune system.

5.2. Pharmacokinetic properties

IRON

Absorption

The rate of iron absorption from food and supplements is variable depending on the individual and iron demand. Ascorbic acid in the duodenum aids in the absorption of non-haem iron.

Distribution

Most of the iron in the human body is incorporated into haemoglobin with the remainder stored as ferritin or hemosiderin in the bone marrow, liver, spleen, or muscle (myoglobin). Iron is transported in the body by binding reversibly to transferrin.

Excretion

Iron is highly conserved in the human body. In the absence of bleeding (including menstruation) or pregnancy, the body loses only a small quantity of iron each day, mostly through the faeces.

VITAMIN C

Absorption

Following oral ingestion, vitamin C is well absorbed at lower dose; however, absorption decreases as the dose increases. Pharmacokinetic studies have revealed that approximately 87 % of a 30-mg oral dose is absorbed, 80 % of a 100-mg dose, 63 % of a 500 mg dose, and less than 50 % of a 1 250-mg dose. This is a result of vitamin C being transported from the intestines to the venous circulation by the sodium-dependent vitamin C transporter (SVCT1), which is saturable. The decreased bioavailability of vitamin C with increased dosages, along with increased renal excretion, limits the plasma levels attainable with oral vitamin C supplementation.

Elimination

Most vitamin C that is absorbed is excreted in the urine.

FOLIC ACID

Absorption

Folic acid from supplements is almost 100 % bioavailable.

Biotransformation

After absorption, folic acid is reduced to tetrahydrofolate before it enters a methylation cycle where it is converted to L-methylfolate.

Elimination

Excretion of folic acid is mainly via the urine, but it is also present in faeces.

VITAMIN B12

Absorption

Absorption of vitamin B12 occurs in the terminal ileum via an active transport mechanism which is dependent on the presence of intrinsic factor, a glycoprotein produced in the stomach, and normal gastric pH. In addition, a small percentage of vitamin B12 is also absorbed by passive diffusion. Absorption under fasting conditions is greater than in the postprandial period.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Maize starch

Maltodextrin

Stevia (sweetener – 5 mg per sachet)

Sunflower lecithin

Vanilla flavour

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

2 Years

6.4. Special precautions for storage

Store at or below 25 °C in a cool, dry place protected from light and moisture.

Do not use if the package seal is broken. Do not use damaged or open sachets.

Advise patients not to take FERRITONE after the expiry date stated on the packaging material.

6.5. Nature and contents of container

An off-white powder within a laminated foil sachet packed within an outer carton.

Pack size: 30 sachets

6.6. Special precautions for disposal and other handling

FERRITONE should not be disposed of in drains or sewerage systems.

Advise patients to return all unused medicine to their pharmacist for disposal.

7. HOLDER OF THE CERTIFICATE OF REGISTRATION

MC Pharma (Pty) Ltd

62 Constantia Avenue

Mnandi

Pretoria

0157

8. REGISTRATION NUMBER(S):

To be allocated by the Authority upon registration.

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be allocated by the Authority upon registration.

10. DATE OF REVISION OF THE TEXT

23 September 2025