# SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

## 1. NAME OF THE MEDICINAL PRODUCT

Hifer C Kit Tablets

Each combikit contains:

- 1 oval white tablet of Calcium, Magnesium, Zinc and Vitamin D3.
- 1 round brown tablet of Carbonyl Iron, Folic Acid, Vitamin C, Vitamin B12 and Zinc.

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredients: Calcium, Magnesium, Zinc and Vitamin D3; Carbonyl Iron, Folic Acid, Vitamin C, Vitamin B12 and Zinc.

For the full list of excipients, see section 6.1.

| Component | Description |
|---|---|
| Calcium, Magnesium, Zinc and Vitamin D3 tablet | White, oval, caplet-shaped, film-coated, scored tablet. |
| Carbonyl Iron, Folic Acid, Ascorbic Acid, Vitamin B12 and Zinc tablet | Chocolate brown coloured, circular, biconvex, scored, film-coated tablet. |

## 3. PHARMACEUTICAL FORM

Oral solid dosage form: film-coated tablets.

Calcium, Magnesium, Zinc and Vitamin D3 Tablets: white, oval, caplet-shaped, film-coated, scored tablets.

Carbonyl Iron, Folic Acid, Ascorbic Acid, Vitamin B12 and Zinc Tablets: chocolate brown coloured, circular, biconvex, scored, film-coated tablets.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

Hifer C Kit is indicated for increased iron and calcium needs in pregnancy and lactation, and for nutritional deficiency of calcium and iron in adults.

Calcium and iron needs and absorption increase during growth, pregnancy, menstruation, lactation and in blood disorders. Absorption is increased markedly when calcium and iron needs are acute, such as in haemorrhage or anaemias.

Iron deficiency anaemia in pregnancy: dietary absorption of iron in pregnancy and iron stores of women of childbearing age are widely considered insufficient to meet the high demands for iron in pregnancy, thereby justifying iron supplementation. Iron deficiency anaemia is more common in women with high parity, history of menorrhagia or multiple gestations, women with diets low in meat and ascorbic acid, and pregnant women. The World Health Organization defines anaemia in pregnancy as haemoglobin concentration below 110 g/L during the first and third trimesters and below 105 g/L during the second trimester, or haematocrit less than 32%.

Iron supplements are effective in improving the haematological and iron status of the mother. Improvement in iron status depends on the form of supplemental iron and the dose. Higher cord serum ferritin levels have been reported in infants of iron-replete mothers compared to iron-deficient mothers. High cord serum ferritin indicates larger iron reserves at birth and reduces the risk of iron deficiency during infancy. Routine iron supplementation raises and maintains serum ferritin.

In Hifer C Kit, the Calcium, Magnesium, Zinc and Vitamin D3 tablet is indicated for:

- Formation of healthy bones and teeth.
- Normal function of nerves and muscles.
- Heart function.
- Normal structure and function of cell membranes.
- Clotting of blood.
- Actions of many hormones.
- Phagocytic activity of white blood cells.

Calcium is an essential element required for proper nervous and musculoskeletal system function, cell-membrane and capillary permeability, and activation of enzymatic reactions.

Magnesium is used as a cofactor in a variety of enzyme systems and plays a role in muscular excitement and neurochemical transmission.

Zinc is a necessary nutritional supplement required by over 200 metalloenzymes for proper function. Zinc-dependent physiological processes include sexual maturation and reproduction, cell growth and division, vision, night vision, wound healing, immune response and taste acuity. In pregnant women it reduces the incidence of miscarriage, labour complications and low birth weight babies.

Vitamin D is useful in reducing bone loss and fracture incidence in the elderly and may be helpful in preventing or limiting some perinatal growth retardation and in some cases of psoriasis.

In Hifer C Kit, the Carbonyl Iron, Folic Acid, Vitamin C, Vitamin B12 and Zinc tablet is indicated for:

- Formation of haemoglobin.
- Development and maturation of red blood cells.
- Oxygen carriage in the blood in the form of haemoglobin.
- Tissue oxidation.
- Supply of oxygen to muscle.
- Chromatin of the nucleus contains iron.
- Oxidation in nerve cells.

Iron, as a constituent of haemoglobin, plays an essential role in oxygen transport. Deficiency of iron leads to anaemia.

Folic acid is reduced in the body to tetrahydrofolate, a co-enzyme involved in various metabolic processes including DNA synthesis. Deficiency of folic acid leads to megaloblastic anaemia.

Vitamin C is required as a dietary source and acts as a cofactor in numerous biological processes. It is important in collagen formation, hydroxylation reactions, iron incorporation into ferritin, phagocytic function of leucocytes, anti-inflammatory activity and wound healing. Deficiency may produce scurvy and anaemia.

Vitamin B12 occurs mainly as methylcobalamin, adenosylcobalamin and hydroxocobalamin, acting as co-enzymes in several metabolic pathways. Deficiency interferes with haemopoiesis and produces megaloblastic anaemia.

Zinc sulphate is a constituent of many enzymes and is essential to the body. It is present with insulin in the pancreas and plays a role in DNA synthesis and cell division.

## 4.2 Posology and method of administration

The recommended dose of Hifer C Kit is 1 kit per day; however, the dose may be increased only if prescribed by the doctor.

Each combikit contains:

- (A) 1 oval white tablet of Calcium, Magnesium, Zinc and Vitamin D3 to be taken in the morning. It is recommended to take the dose within one and a half hours of a meal with a glass of water.
- (B) 1 round brown tablet of Carbonyl Iron, Folic Acid, Vitamin C, Vitamin B12 and Zinc to be taken in the afternoon. It is recommended to take the dose with a full glass of water. Carbonyl iron should be taken on an empty stomach for best results. If stomach upset occurs, take the preparation with food or following a meal.

Method of administration: Oral.

## 4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients of the tablets.
- Diseases and/or conditions resulting in hypercalcaemia and/or hypercalciuria, such as myeloma, bone metastases or other malignant bone disease, sarcoidosis, or primary hyperparathyroidism.
- Nephrolithiasis or nephrocalcinosis.
- Severe renal impairment and renal failure.
- Hypervitaminosis D.
- Relative contraindications include osteoporosis due to prolonged immobilisation, renal stones and severe hypercalciuria.
- Calcium is contraindicated in patients with ventricular fibrillation or hypercalcaemia and should be used cautiously in patients receiving digitalis glycosides or with cardiac or renal disease.
- Magnesium is contraindicated in patients with myocardial damage or heart block and should be given with caution in patients with impaired renal function.
- Zinc supplementation should be carefully considered before administration to patients with copper deficiency.
- Vitamin D is contraindicated in patients with hypercalcaemia, evidence of vitamin D toxicity or hypersensitivity to any component of a vitamin D-containing product.
- Not recommended in haemochromatosis or haemosiderosis.

## 4.4 Special warnings and precautions for use

Keep this medicine out of the reach of children. Accidental overdose is a leading cause of fatal poisoning in children. In case of accidental overdose, the patient should be hospitalised and given general supportive measures.

Patients already taking thiazide diuretics and/or cardiac glycosides should be referred to their doctor prior to concomitant use. Concomitant use should be prescribed with caution due to the increased risk of hypercalcaemia.

During long-term treatment, serum calcium levels should be followed and renal function monitored through measurements of serum creatinine. Monitoring is especially important in elderly patients on concomitant cardiac glycosides or diuretics and in patients with a high tendency to calculus formation. In case of hypercalcaemia

or signs of impaired renal function, the dose should be reduced or treatment discontinued. Treatment should be reduced or interrupted temporarily if urinary calcium exceeds 7.5 mmol/24 h (300 mg/24 h).

Vitamin D should be used with caution in patients with impaired renal function and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be considered. In patients with severe renal insufficiency, vitamin D in the form of colecalciferol is not metabolised normally and other forms of vitamin D should be used.

Calcium, Magnesium, Zinc and Vitamin D3 tablet should be prescribed with caution in patients suffering from sarcoidosis due to the risk of increased metabolism of vitamin D into its active form. These patients should be monitored with regard to calcium content in serum and urine.

The product should be used with caution in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

The content of vitamin D should be considered when prescribing other medicinal products containing vitamin D. Additional doses of calcium or vitamin D should be taken under close medical supervision. Serum calcium levels and urinary calcium excretion should be monitored frequently. Milk-alkali syndrome, i.e. hypercalcaemia, alkalosis and renal impairment, can develop when large amounts of calcium are ingested with absorbable alkali.

Allowances should be made for calcium and vitamin D supplements from other sources. Some antacids may decrease absorption of iron salts.

Iron compounds should not be given to patients receiving repeated blood transfusions or to patients with anaemias not caused by iron deficiency unless iron deficiency is also present. Oral iron therapy should not be administered concomitantly with parenteral iron. Caution is required in patients with iron storage or iron absorption disease, haemoglobinopathies or existing gastrointestinal disease.

Folic acid should never be given alone, or with inadequate vitamin B12, for the treatment of undiagnosed megaloblastic anaemia, since folic acid may produce a haematopoietic response without preventing worsening neurological symptoms due to vitamin B12 deficiency. Caution is advised in patients who may have folate-dependent tumours.

Ascorbic acid is usually well tolerated; large doses may cause diarrhoea and other gastrointestinal disturbances.

Cyanocobalamin hypersensitivity reactions have occurred rarely. If possible, it should not be given without first confirming the diagnosis and should not be used to treat megaloblastic anaemia of pregnancy.

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

- Concomitant use of proton pump inhibitors and calcium carbonate can decrease absorption of calcium salts.
- Thiazide diuretics reduce urinary excretion of calcium; serum calcium should be regularly monitored during concomitant use.
- Concomitant intake of levothyroxine and calcium carbonate may reduce levothyroxine absorption and increase serum thyrotropin levels.
- Systemic corticosteroids reduce calcium absorption; dose adjustment of calcium, magnesium, zinc and vitamin D supplements may be necessary.

- Concomitant intake of penicillamine and zinc may depress zinc absorption.
- Cholestyramine and vitamin D may reduce absorption of vitamin D.
- Ion exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce gastrointestinal absorption of vitamin D.
- Tetracyclines should be administered at least two hours before or four to six hours after calcium, magnesium, zinc and vitamin D supplements.
- Hypercalcaemia may increase toxicity of cardiac glycosides; patients should be monitored by ECG and serum calcium levels.
- Bisphosphonates or sodium fluoride should be administered at least three hours before calcium, magnesium, zinc and vitamin D supplements.
- Rifampicin, phenytoin or barbiturates may reduce activity of vitamin D3 by increasing metabolism.
- Quinolone antibiotic absorption may be impaired by calcium and should be taken two hours before or six hours after calcium.
- Calcium salts may decrease absorption of iron; the iron preparation should be taken at least two hours away from calcium.
- Calcium salts may reduce absorption of estramustine or thyroid hormones; administration should be spaced by at least two hours.
- Phenobarbital and phenytoin may reduce plasma levels of 25-hydroxyvitamin D.
- Oxalic acid, phosphate and phytic acid may inhibit calcium absorption; calcium products should not be taken within two hours of foods high in oxalic acid and phytic acid.
- Folic acid can reduce the plasma concentration of phenytoin.
- Oral iron and zinc sulphate reduce absorption of tetracyclines.

**4.6 Fertility, pregnancy and lactation**

Hifer C Kit may be administered during pregnancy and lactation on the recommendation of the physician. There are no data available on the effect of Hifer C Kit on fertility.

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

There are no data on the effect of this product on the ability to drive or use machines; however, an effect is unlikely.

## 4.8 Undesirable effects

The following adverse effects are reported by component and by system organ class where applicable.

Calcium: Hypercalcaemia may be associated with calcium therapy, particularly in patients with cardiac or renal disease. Other effects include gastrointestinal irritation and/or constipation after oral administration. Too rapid intravenous injection of calcium can cause hypotension, cardiac arrhythmias and cardiac arrest.

Magnesium: Adverse effects are generally the result of magnesium overdosage and may include drowsiness or other CNS depressant effects, muscular weakness, bradycardia, hypotension, respiratory depression and increased QT intervals on ECG. Very high magnesium levels may cause neuromuscular blocking activity and eventually cardiac arrest.

Zinc: Large doses may cause gastrointestinal disturbances. Haematological abnormalities may occur with large doses, particularly if coexistent copper deficiency exists.

Vitamin D: Chronic high doses may cause hypercalcaemia. Early symptoms include nausea, vomiting, weakness, headache, somnolence, dry mouth, constipation, metallic taste, muscle pain and bone pain. Late symptoms may include polyuria, polydipsia, anorexia, weight loss, nocturia, conjunctivitis, pancreatitis, photophobia, rhinorrhoea, pruritus, hyperthermia, decreased libido, elevated BUN, albuminuria, hypercholesterolaemia, elevated ALT and AST, ectopic calcification, nephrocalcinosis, hypertension and cardiac arrhythmias.

| **System Organ Class** | **Frequency** | **Undesirable effects** |
|---|---|---|
| Immune system disorders | Not known | Hypersensitivity reactions including pruritus, wheezing, urticaria and oropharyngeal swelling have been reported in the post-marketing environment. |
| Metabolism and nutrition disorders | Uncommon | Hypercalcaemia and hypercalciuria. |
| Metabolism and nutrition disorders | Very rare | Milk-alkali syndrome, usually seen only in overdose. |
| Gastrointestinal disorders | Rare | Constipation, flatulence, nausea, abdominal pain and diarrhoea. |
| Gastrointestinal disorders | Very rare | Dyspepsia. |
| Skin and subcutaneous tissue disorders | Rare | Pruritus, rash and urticaria. |
| Special population: renal impairment | Not known | Potential risk of hyperphosphataemia, nephrolithiasis and nephrocalcinosis. |

Iron: The astringent action of iron may produce gastrointestinal irritation and abdominal pain with nausea and vomiting. Other gastrointestinal side effects include diarrhoea or constipation; these may be reduced by administration with or after food.

Folic acid: Generally well tolerated. Gastrointestinal disturbances may occur and hypersensitivity reactions have been reported rarely.

Ascorbic acid: Large doses have resulted in haemolysis in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency.

Cyanocobalamin: Aminoglycosides, aminosalicylic acid, anticonvulsants, biguanides, chloramphenicol, cimetidine, colchicine, potassium salts and methyldopa may reduce absorption from the gastrointestinal tract. Serum concentrations may be decreased by concurrent administration of oral contraceptives.

Zinc: Prolonged use may lead to copper deficiency and anaemia, which has responded to withdrawal of zinc and symptomatic therapy. Metal fume fever, with nausea, dyspnoea and chest pain, follows inhalation of zinc-containing dust.

Reporting suspected adverse reactions after authorisation of the medicinal product is important. Healthcare professionals are asked to report any suspected adverse reactions via the PPB website: https://pv.pharmacyboardkenya.org

### 4.9 Overdose

No cases of overdosage have been reported.

Calcium: Oral overdoses of calcium-containing products are unlikely to cause hypercalcaemia unless other drugs are given concurrently that enhance calcium absorption. Hypercalcaemia should be treated by withholding calcium therapy and other calcium-elevating drugs. Mild hypercalcaemia generally resolves without further intervention when renal function is adequate.

Magnesium: Treatment of hypermagnesaemia depends on serum magnesium level and associated clinical effects. Ventilatory support and intravenous calcium may be required for severe hypermagnesaemia.

Zinc: Signs of zinc overdose include haemolytic anaemia, hypotension, jaundice, vomiting and pulmonary oedema. Treatment may include removal of the source, dilution with milk or water and chelation therapy using calcium disodium edetate.

Vitamin D: Hypercalcaemia can result from excess intake of prescribed forms of vitamin D or high amounts of vitamin D. Hypercalcaemia associated with hypervitaminosis D may cause multiple debilitating effects, including anorexia, nausea, vomiting, polyuria and polydipsia.

Iron: Symptoms may include nausea, vomiting, diarrhoea, abdominal pain, haematemesis, rectal bleeding, lethargy and circulatory collapse. Hyperglycaemia and metabolic acidosis may also occur. Symptomatic treatment should be initiated immediately, and further absorption should be minimised or prevented.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

The pharmacological effects of the vitamins and minerals in the Calcium, Magnesium, Zinc and Vitamin D3 tablet are summarised below. Vitamin D increases the intestinal absorption of calcium. Administration of calcium and vitamin D3 counteracts the increase of parathyroid hormone caused by calcium deficiency, which causes increased bone resorption.

The pharmacological effects of the vitamins and minerals in the Carbonyl Iron, Folic Acid, Vitamin C, Vitamin B12 and Zinc tablet relate to correction or prevention of deficiencies of the respective constituents.

### 5.2 Pharmacokinetic properties

Calcium is absorbed through the gastrointestinal tract. About 99% of body calcium is concentrated in bones and teeth, while the remainder is present in intra- and extracellular fluids. Calcium is eliminated through faeces, urine and sweat.

Magnesium is about 30-35% bound to proteins and the remainder exists as free ions. It is excreted by the kidneys at a rate proportional to the serum concentration and glomerular filtration.

Zinc is absorbed principally from the duodenum and ileum. Bioavailability depends on the food in which it is present. Zinc is stored mostly in red and white blood cells, muscle, skin, bone, retina, pancreas, liver, kidney and prostate. Elimination is primarily via faeces, with some excretion by the kidneys and in sweat.

Vitamin D is absorbed in the small intestine, circulates bound to a specific globulin, is converted in the liver and kidneys to active metabolites, stored in adipose and muscle tissues and excreted in faeces and urine.

Carbonyl iron requires solubilisation by gastric acid for absorption. It is retained in the stomach and slowly solubilised, behaving like a sustained-release iron preparation. Iron is irregularly and incompletely absorbed from the gastrointestinal tract, mainly in the duodenum and jejunum.

Folic acid is absorbed mainly from the proximal small intestine, appears rapidly in blood, is extensively bound to plasma proteins, distributed in tissues, excreted in urine and stored in the liver as folate.

Ascorbic acid is readily absorbed from the gastrointestinal tract and widely distributed in body tissues. Excess ascorbic acid is rapidly eliminated in urine.

Cyanocobalamin is absorbed from the gastrointestinal tract and extensively bound to specific plasma proteins. Cobalamins are stored in the liver, excreted in bile and undergo enterohepatic recycling. Part of a dose is excreted in urine.

Zinc sulphate is poorly absorbed from the gastrointestinal tract, widely distributed throughout the body and excreted in faeces, with traces in urine.

### 5.3 Preclinical safety data

Preclinical safety data do not add anything of further significance to the prescriber.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Calcium, Magnesium, Zinc and Vitamin D3 Tablet: Croscarmellose Sodium; Microcrystalline Cellulose; Maize Starch; Pregelatinised Starch; Copovidone (PVP K30); Sodium Methylparaben; Sodium Propylparaben; Purified Talc; Magnesium Stearate; Sodium Starch Glycolate; Sodium Lauryl Sulphate.

Carbonyl Iron, Folic Acid, Vitamin C, Vitamin B12 and Zinc Tablet: Calcium Carbonate; Copovidone (PVP K30); Microcrystalline Cellulose; Dibasic Calcium Phosphate; Talc; Magnesium Stearate; Croscarmellose Sodium; Unique Coat FCNAQ; Colour: Iron Oxide Red.

### 6.2 Incompatibilities

No major incompatibilities are known.

### 6.3 Shelf life

24 months. The medication should not be used after the expiration date printed on the package.

### 6.4 Special precautions for storage

Store below 30°C. Protect from light and moisture. Store in the original package. Keep out of the reach of children.

### 6.5 Nature and contents of container

Aluminium-PVC blister strip.

Pack size: each pack contains 30 combikits for 30 days.

Each kit contains 1 oval white tablet of Calcium, Magnesium, Zinc and Vitamin D3 (morning dose) and 1 round brown tablet of Carbonyl Iron, Folic Acid, Vitamin C, Vitamin B12 and Zinc (afternoon dose).

### 6.6 Special precautions for disposal and other handling

No special requirements. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION

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## 8. MARKETING AUTHORISATION NUMBER

Hifer C Kit – H2015/CTD4019/500

## 9. DATE OF FIRST REGISTRATION / RENEWAL OF THE REGISTRATION

Date of first authorisation: 14/10/2015.

Date of latest renewal: 20/12/2022.

## 10. DATE OF REVISION OF THE TEXT

31/10/2023