1. Name of the medicinal product

Zegem Capsule

2. Qualitative and quantitative composition

Each capsule contains 50mg Iron Polymaltose, 250mg Folic Acid, 7.5mcg

Zinc and 27.5mg Vitamin B12.

3. Pharmaceutical form

Soft gel Capsule

4. Clinical particulars

4.1 Therapeutic indications

Zegem Capsule is indicated for the prevention and treatment of iron-deficiency anaemia, particularly when associated with deficiencies in folic acid, vitamin B12, and zinc. It is suitable for use in the following situations:

1. Nutritional anaemia due to inadequate dietary intake of iron, folic acid, vitamin B12, or zinc.
2. Pregnancy and lactation, where increased requirements of iron, folic acid, and vitamin B12 may lead to deficiency.
3. Convalescent states, where recovery from illness or blood loss may necessitate replenishment of these nutrients.
4. Other clinical conditions where combined iron, folic acid, vitamin B12, and zinc supplementation is considered beneficial under medical supervision.

4.2 Posology and method of administration

Posology

- Adults: equivalent to 100 mg iron once daily, or as directed by a physician.
- Children (6–12 years): 50 mg iron once daily, or as prescribed.
- Children under 6 years: Use only under medical supervision; dose should be adjusted according to weight and severity of deficiency.
- Pregnant and lactating women: 100 mg iron once daily, unless otherwise directed by a healthcare professional.

Method of Administration

- Zegem Capsule is for oral use only.
- It may be taken before or after meals; if gastrointestinal discomfort occurs, it is preferable to take after food..
- The dosing schedule should be maintained consistently to ensure optimal replenishment of iron, folic acid, vitamin B12, and zinc.

Special populations

- Renal or hepatic impairment: Dose adjustment may be necessary; use under supervision.
- Elderly: Use standard adult dosing unless clinical condition suggests otherwise.

4.3 Contraindications

1. Hypersensitivity to any component of Zegem Capsule, including iron polymaltose, folic acid, vitamin B12, or zinc.
2. Patients with haemochromatosis, hemosiderosis, or other iron overload disorders.
3. Vitamin B12 hypersensitivity or known folic acid-related disorders (e.g., megaloblastic anemia of other origin than folate/B12 deficiency).

4.4 Special warnings and precautions for use

General precautions:

- Monitor haematological parameters (hemoglobin, hematocrit, ferritin) during prolonged therapy to avoid iron overload.
- Use with caution in patients with renal or hepatic impairment, as metabolism and excretion of vitamins and minerals may be affected.
- Iron supplementation can mask symptoms of underlying medical conditions, such as gastrointestinal bleeding or chronic diseases causing anemia.
- Patients with a history of allergies to iron compounds, folic acid, vitamin B12, or zinc should use this product under medical supervision.

Children:

- Accidental overdose is a serious risk: Children are particularly vulnerable to iron toxicity; even a few capsules or doses can be fatal.
- Keep the capsule out of reach of children and in a child-resistant container.
- Dosing must be carefully measured using a calibrated spoon or cup to avoid overdose.
- Children with known metabolic disorders affecting iron, vitamin B12, or folate metabolism should only use Zegem under medical supervision.

Other considerations:

- Patients with conditions leading to iron accumulation (e.g., hemochromatosis, hemosiderosis) should not use Zegem, as supplementation may worsen iron overload.
- Patients on chelation therapy should avoid concomitant iron supplementation unless advised by a physician.
- Use cautiously in patients receiving antibiotics such as tetracyclines or fluoroquinolones, as iron may reduce their absorption.

Storage and handling:

- Store at room temperature away from moisture and heat.

4.5 Interaction with other medicinal products and other forms of interaction

Iron (Ferric Ammonium Citrate) Interactions:

- Antacids, calcium, and magnesium-containing products may reduce the absorption of iron. It is recommended to administer iron at least 2 hours before or after these products.
- Tetracycline and fluoroquinolone antibiotics (e.g., ciprofloxacin, doxycycline) may form insoluble complexes with iron, reducing absorption of both the antibiotic and iron. A separation of 2–3 hours between doses is recommended.
- Levothyroxine absorption may be reduced if taken concurrently with iron; doses should be separated by at least 4 hours.

Folic Acid Interactions:

- Methotrexate (high-dose chemotherapy): Folate supplementation may reduce the cytotoxic efficacy of methotrexate. In lower doses (e.g., for rheumatoid arthritis), folate supplementation reduces toxicity without compromising efficacy.
- Anticonvulsants (such as phenytoin and phenobarbital) may increase folate metabolism, potentially reducing the effectiveness of folic acid supplementation.

Vitamin B12 (Cyanocobalamin) Interactions:

- Chloramphenicol may antagonize the hematologic effects of vitamin B12, reducing erythropoiesis.
- Metformin (long-term therapy) may reduce vitamin B12 absorption, which may require monitoring and supplementation.

Zinc Interactions:

- High doses of zinc may interfere with copper absorption, potentially causing copper deficiency during prolonged therapy.
- Zinc may also reduce the absorption of tetracycline antibiotics; doses should be separated appropriately.

Other Forms of Interaction:

- Laboratory tests: Iron therapy may interfere with certain biochemical tests, including serum iron, ferritin, and total iron-binding capacity.
- Concurrent supplementation: The combined use of Zegem with other multivitamin or mineral preparations may lead to excessive intake of iron, folic acid, vitamin B12, or zinc, increasing the risk of adverse reactions.

Practical recommendations:

- Administer Zegem at different times from interacting medications to minimize absorption interference.
- Monitor hematological and biochemical parameters during prolonged therapy or in patients on multiple supplements/medications.

4.6 Fertility, pregnancy and lactation

Fertility:

- No adverse effects on fertility have been reported at recommended doses of Zegem Capsule.
- Iron, folic acid, vitamin B12, and zinc supplementation do not negatively affect reproductive function when used appropriately.

Pregnancy:

- Zegem Capsule is recommended for use during pregnancy when indicated, particularly for the prevention and treatment of iron-deficiency anemia and associated folate and vitamin B12 deficiencies.
- Adequate folic acid supplementation during pregnancy helps prevent neural tube defects in the developing fetus.
- Iron supplementation supports increased maternal blood volume and prevents maternal anemia, reducing the risk of preterm delivery and low birth weight.
- Precautions: Monitor maternal hematological parameters. Avoid excessive iron intake, as it may cause gastrointestinal discomfort.

Lactation:

- Zegem Capsule can be safely used during breastfeeding when supplementation is required.
- Iron, folic acid, vitamin B12, and zinc are excreted in breast milk in small amounts that are generally considered safe for the infant and may help maintain adequate nutrient levels in the breastfeeding infant.
- Ensure that maternal dosing does not exceed recommended levels to avoid potential gastrointestinal side effects.

General Advice:

- Use under the supervision of a healthcare professional.
- Regular monitoring is advised if prolonged therapy is necessary

4.7 Effects on ability to drive and use machines
Zegem Capsule has no influence on the ability to drive and use machines.

4.8 Undesirable effects
Very common (≥1/10):
- Gastrointestinal discomfort (nausea, abdominal pain)

Common (≥1/100 to <1/10):
- Constipation
- Diarrhea
- Dark-colored stools (due to iron)

Uncommon (≥1/1,000 to <1/100):
- Flatulence

4.9 Overdose

Symptoms

- Iron overdose is potentially life-threatening, particularly in children.
- Symptoms may include vomiting, diarrhea, abdominal pain, gastrointestinal bleeding, hypotension, metabolic acidosis, shock, and in severe cases, organ failure.
- Vitamin B12, folic acid, and zinc overdose is rare but may cause nausea, diarrhea, or neurologic symptoms if taken in extremely high doses.

5 Pharmacological properties

5.1 Pharmacodynamic properties

1. Iron (Ferric Ammonium Citrate)
    - Iron is a key hematinic: it is essential for erythropoiesis (red blood cell production) and hemoglobin synthesis.
    - The citrate moiety helps solubilize ferric (Fe^{3+}) iron, improving its availability and absorption in the gastrointestinal tract.
    - Once absorbed, iron replenishes body iron stores and supports oxygen-carrying capacity via hemoglobin.
    - (Interesting) Ferric ammonium citrate has also been shown in research to have antiviral effects in vitro, by inhibiting certain viruses.
2. Folic Acid (Vitamin B9)
    - Folic acid is converted in the body to tetrahydrofolate (THF) derivatives via dihydrofolate reductase.
    - These active folate forms are essential for purine and thymidylate synthesis, so they support DNA and RNA synthesis.
    - Folic acid works especially during periods of rapid cell division (e.g., in the bone marrow) to support red blood cell maturation.
    - Also, with vitamin B12, folate participates in the remethylation of homocysteine to methionine via methionine synthase.
3. Cyanocobalamin (Vitamin B12)
    - Cyanocobalamin is a synthetic form of vitamin B12.
    - It acts as a cofactor for methionine synthase, which is crucial in the conversion of homocysteine to methionine – a reaction tied to DNA synthesis and methylation.

- Also, as adenosylcobalamin, it helps convert methylmalonyl-CoA to succinyl-CoA, a reaction important in energy metabolism (fat and protein metabolism) and red blood cell formation.
- By supporting DNA synthesis and red cell maturation, B12 helps correct megaloblastic anemia.

4. Zinc
    - Although less often detailed in standard “pharmacodynamic” descriptions compared to iron, folate, B12 — zinc is an essential trace element. In the context of Zegem, zinc likely supports immune function, protein synthesis, and may help in wound healing or cell division (all relevant in states of deficiency).
    - (Note: Specific detailed PD of zinc in Zegem Capsule may not be well characterized in publicly available SmPC, but its inclusion suggests a role in correcting zinc deficiency and supporting overall hematopoiesis and cellular health.)

Integrated Pharmacodynamic Effect of Zegem

- Correction of Anemia: By providing iron, folic acid, and B12, Zegem synergistically helps treat different types of anemia—particularly iron-deficiency anemia and megaloblastic (macrocytic) anemia.
- Support of Hematopoietic System: The combined action on DNA synthesis (via folate and B12) and hemoglobin production (via iron) promotes effective erythropoiesis.
- Cell Division & Growth: Folic acid and B12 support rapidly dividing cells (bone marrow, epithelial cells) because of their roles in nucleotide synthesis.
- Immune and General Cellular Function: Zinc contributes to immune function and various enzymatic processes, which help in recovery from deficiency states.

5.2 Pharmacokinetic properties

1. Iron (Ferric Ammonium Citrate)
    - Absorption: Iron is absorbed irregularly and incompletely from the GI tract, with the duodenum and jejunum being the main sites.
    - Factors influencing absorption: Acid environment of the stomach and dietary acids (e.g., ascorbic acid) help absorption.
    - The body’s iron status matters: absorption *increases* in iron-deficiency states or fasting, and *decreases* when iron stores are overloaded.
    - Transport & Distribution: Once absorbed, most iron is bound to transferrin, transported to bone marrow for incorporation into hemoglobin.
    - Storage: Excess iron (not immediately used) is stored in ferritin and hemosiderin in tissues.
    - Excretion: Very little elemental iron is excreted; most iron from hemoglobin breakdown is recycled.
2. Folic Acid (Vitamin B9)
    - Absorption: Rapidly absorbed from the GI tract, mainly in the duodenum and jejunum.

- Metabolism / Conversion: Once absorbed, it is converted (in plasma and liver) into its active form, 5-methyltetrahydrofolate.
- Distribution: The liver is the main storage site for folates, and folate is also concentrated in the cerebrospinal fluid (CSF).
- Enterohepatic recycling: Folate undergoes enterohepatic circulation.
- Elimination: Metabolites are eliminated in urine; excess unmodified folic acid is also excreted unchanged in urine. Folate is also excreted in breast milk.
- Removal by dialysis: Folic acid can be removed by hemodialysis.

3. Cyanocobalamin (Vitamin B12)
   - Absorption: B12 binds to intrinsic factor (secreted by gastric mucosa) and is then actively absorbed in the GI tract.
   - Passive absorption: Some absorption can also occur via passive diffusion (especially at high doses).
   - Plasma Binding: Once absorbed, B12 binds extensively to transcobalamin proteins (especially transcobalamin II), which help transport it to tissues.
   - Storage: B12 is stored in the liver.
   - Enterohepatic Recycling: There is significant recycling via the bile.
   - Excretion: Part of administered B12 is excreted in the urine (a good fraction within the first ~8 hours), but urinary excretion accounts for only a small fraction of total body B12 stores.
   - Distribution to special compartments: It crosses the placenta and appears in breast milk.
4. Zinc
   - Zinc from oral formulations is absorbed in the small intestine, distributed to tissues, and excess zinc is excreted mostly via the GI tract (feces) and to a lesser extent in urine (depending on the form).

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SMPC.

6 Pharmaceutical particulars

6.1 List of excipients

Folic Acid

Zinc

Vitamin B12

Iron Polymaltose

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

None stated.

6.5 Nature and contents of container

Alu-PVC Blister Pack

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

7 Marketing authorisation holder

Zolon Healthcare Limited, Block A, Aswani Market Road, Isolo Lagos

- Manufacturer: EMZOR PHARMACEUTCAL INDUSTRIES LIMITED, Flowergate Mixed Development Scheme,Km 1 Sagamu/Benin Expressway,Sagamu,Ogun State.

8. Marketing authorisation number(s)

A11-100375

9 Date of first authorisation/renewal of the authorisation

N/A

10 Date of revision of the text

February 9th,2024