1. **GENERIC NAME**

Capsules of Vitamins B-Complex and C with Zinc Sulphate Monohydrate

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each capsule contains:

- Zinc Sulphate Monohydrate IP 41.4 mg (equivalent to 15 mg elemental zinc)
- Thiamine Mononitrate IP 10 mg
- Vitamin B₂ IP 10 mg
- Nicotinamide IP 100 mg
- Vitamin B₆ IP 3 mg
- Vitamin B₁₂ IP 15 mcg
- Calcium Pantothenate IP 50 mg
- Vitamin C IP 150 mg
- Folic Acid IP 1500 mcg
- Biotin USP 100 mcg

Colours: Approved colours used in empty capsule shell q.s.

(Appropriate overages included for vitamins)

3. **DOSAGE FORM AND STRENGTH**

Hard Gelatin Capsules for oral administration.

Each capsule contains:

- Zinc Sulphate Monohydrate IP 41.4 mg (equivalent to 15 mg elemental zinc)
- Thiamine Mononitrate IP 10 mg
- Vitamin B₂ IP 10 mg
- Nicotinamide IP 100 mg
- Vitamin B₆ IP 3 mg
- Vitamin B₁₂ IP 15 mcg
- Calcium Pantothenate IP 50 mg
- Vitamin C IP 150 mg
- Folic Acid IP 1500 mcg
- Biotin USP 100 mcg

Colours: Approved colours used in empty capsule shell q.s.

(Appropriate overages included for vitamins)

4. **CLINICAL PARTICULARS**

4.1 Therapeutic Indications

**ZEVIT** is indicated for the treatment of vitamin B-complex, vitamin C and zinc deficiency states in adults which may be associated with the following conditions:

- Dietary restrictions: in conditions such as obesity, cardiovascular diseases, chronic diarrhoea or dysentery, diabetes mellitus etc.
- Malnutrition
- Infections or recovering from infections
- Long term antibiotic use

4.2 Posology and Method of Administration
**Route of Administration**

For oral use.

**Adults**

One capsule once daily.

Duration of treatment depends on the improvement of the deficiency states.

**Children**

*ZEVIT* is not recommended for paediatric use.

**Elderly**

There are no relevant data available.

**Renal Impairment**

Caution should be exercised when administering *ZEVIT* to patients with renal disorders.

**Hepatic Impairment**

Caution should be exercised when administering *ZEVIT* to patients with hepatic disorders.

4.3 **Contraindications**

*ZEVIT* is contraindicated in:

- Hypersensitivity to any of the components.

4.4 **Special Warnings and Precautions for Use**

**Vision disorders**

Cyanocobalamin (vitamin B₁₂) should not be used for Leber's disease or tobacco amblyopia since these optic neuropathies may degenerate further.

**Investigations**

Large doses of riboflavin (vitamin B₂) result in a bright yellow discoloration of the urine that may interfere with certain laboratory tests.

Ascorbic acid, a strong reducing agent, interferes with laboratory tests involving oxidation and reduction reactions. Falsely-elevated or false-negative test results may be obtained from plasma, faeces, or urine samples depending on such factors as the dose of ascorbic acid and specific method used.

**Long-term treatment**

Long-term use of large doses of pyridoxine (vitamin B₆) is associated with the development of severe peripheral neuropathies; the dose at which these occur is not established.

**Treatment preparation and monitoring**

*ZEVIT* should, if possible, not be given to patients with suspected vitamin B₁₂ deficiency without first confirming the diagnosis.

**Tolerance**
Tolerance may be induced with prolonged use of large doses of vitamin C, resulting in symptoms of deficiency when intake is reduced to normal.

Others

High dose of nicotinamide should be used with caution in patients with peptic ulcer disease, gastritis, liver disease, gall bladder disease, diabetes and gout.

4.5 Drug Interactions

Antibiotics

*ZEVIT* decreases the absorption of some fluoroquinolones, tetracyclines and penicillamine derivatives, therefore doses should be separated by at least 3 hours.

Tetracycline antibiotics also decrease zinc absorption, they should therefore be administered 2 hours before or 3 hours after the administration of zinc, in those cases where concomitant use is necessary.

Penicillamine (a chelating agent) may reduce the absorption of zinc.

Penicillamine and antituberculous drugs (such as isoniazid) may increase the requirements for folic acid and pyridoxine (vitamin B6).

Neomycin used orally may reduce the absorption of vitamin B12.

Concomitant use of zinc and quinolones may decrease the absorption of both zinc and the quinolone.

Folic acid antagonists

Folate deficiency states may be produced by folic acid antagonists such as methotrexate, pyrimethamine, triamterene, trimethoprim and sulphonamides such as sulfasalazine.

Oral contraceptives

Serum concentration of vitamin B6, vitamin B12 and folic acid may be decreased by use of oral contraceptives.

Large supplements of vitamin C have been reported to increase serum ethinylestradiol concentrations in women taking oral contraceptives, but a further study showed no effect on either ethinylestradiol or levonorgestrel.

Levodopa

*ZEVIT* contains vitamin B6, which reduces the effects of levodopa, but this does not occur if a dopa decarboxylase inhibitor is also given.

Altretamine

*ZEVIT* contains vitamin B6, which reduces the activity of altretamine.

Antiepileptics

Vitamin B6 and folic acid has been reported to decrease serum concentrations of phenobarbital and phenytoin.

Antiepileptics may produce folate deficiency states.

Serum levels of anticonvulsant drugs may be reduced by the co-administration of folate e.g. folic acid possibly reduces the plasma concentration of phenobarbital, phenytoin and primidone.
Replacement therapy with folinic acid or folic acid may become necessary during antiepileptic therapy in order to prevent megaloblastic anaemia developing.

Concomitant nicotinamide and carbamazepine may decrease carbamazepine clearance.

**Hydralazine**
Hydralazine may increase the requirements for pyridoxine.

**Omeprazole**
Omeprazole has been reported to impair the bioavailability of vitamin B\textsubscript{12} and dietary vitamin C.

**Aluminium-containing antacids**
This medicinal product contains ascorbic acid, which may increase gastrointestinal absorption of aluminium. Concomitant administration of aluminium-containing antacids may affect urinary aluminium elimination. Concurrent administration of antacids and ascorbic acid is not recommended, especially in patients with renal insufficiency.

**Phosphates**
Phosphorus-containing preparations may reduce the absorption of zinc.

**Iron supplements**
The absorption of zinc may be reduced by additionally taken iron supplements.

**Zinc supplements**
Additionally taken zinc supplements reduce the absorption of copper and iron.

**Vitamin C**
As ZEVIT contains vitamin C, it may increase the absorption of iron from the gastrointestinal tract. This should be borne in mind in the case of additional iron supplementation.

**Alcohol**
Alcohol may produce folate deficiency states.

**Fluoride**
As ZEVIT contains calcium (as calcium pantothenate), it reduces the absorption of fluoride, therefore doses should be separated by at least 3 hours.

**Bisphosphonates**
Concomitant intake of a bisphosphonate and zinc may decrease the absorption of both the bisphosphonate and zinc.

**Calcium**
Concomitant calcium intake may decrease zinc absorption.

**Copper**
Concomitant copper intake may decrease zinc absorption.

*L-cysteine, L-histidine, L-methionine, N-acetyl-L-cysteine* (NAC)
Concomitant intake of L-cysteine, L-histidine, L-methionine or NAC may enhance the absorption of zinc. Food, rich in cysteine-containing proteins (i.e. animal muscle tissue) may increase the absorption of zinc if ingested concomitantly.

**Inositol Hexaphosphate**

Concomitant intake of inositol hexaphosphate may decrease the absorption of zinc.

**Caffeine**

Concomitant intake of coffee, caffeinated beverages or caffeine may decrease the absorption of zinc.

**Oxalic acid/Phytic acid**

Concomitant intake of foods rich in oxalic acid (spinach, sweet potatoes, and beans, etc.) or phytic acid (raw beans, seeds, nuts and grains, and soy isolates) may decrease the absorption of zinc.

**Tea**

Concomitant intake of tea (tannins) may decrease the absorption of zinc.

**Raltitrexed**

Concomitant use of folic acid with raltitrexed should be avoided.

**Other**

Absorption of vitamin B₁₂ from the gastrointestinal tract may be reduced by aminosalicylic acid, histamine H₂-antagonists, and colchicine.

4.6 **Use in Special Populations**

**Fertility**

There are no relevant data available.

**Pregnancy**

*ZEVIT* should be administered to pregnant women only after consultation with a physician.

**Lactation**

*ZEVIT* should be administered to breast-feeding mothers only after consultation with a physician.

4.7 **Effects on Ability to Drive and Use Machines**

There are no clinical data proving that *ZEVIT* may have an influence on the ability to drive or use machines.

4.8 **Undesirable Effects**

Multivitamins are generally well tolerated when used within the recommended dose. The following adverse events have been reported with use of ingredients of *ZEVIT*. The frequency of these events cannot be estimated from the available data.

**Immune system disorders**

Hypersensitivity reactions, urticaria, rash, pruritus, anaphylactic reaction

**Gastrointestinal disorders**
Nausea, vomiting, diarrhoea, gastrointestinal discomfort, metallic taste

**Nervous system disorders**

Headache, dizziness, precipitation, exacerbation or prolongation of neurological signs and symptoms of vitamin B\textsubscript{12} deficiency due to folic acid, drowsiness

**Skin and subcutaneous tissue disorders**

Photosensitivity

**Renal and urinary disorders**

Yellow orange discoloration to urine, hyperoxaluria

**Metabolic disorders**

Diabetogenic effects

**4.9 Overdose**

Overdose of ZEVIT can lead to the following symptoms and signs.

**Symptoms and signs**

Diarrhoea, polyuria, sensory neuropathy, peripheral neuropathy, nausea, vomiting, abdominal pain, abdominal cramps, flatulent distension, gastrointestinal obstruction, esophagitis, loss of appetite, breast soreness, photosensitivity, elevations in liver tests and liver damage, including jaundice and parenchymal liver cell injury, headache, dizziness, sleep disturbances, mental changes, other gastrointestinal effects, hyperoxaluria with or without renal failure, formation of renal calcium oxalate calculi. There is a risk of haemolysis if high doses of ascorbic acid are taken.

Decreased HDL has been reported with high doses of zinc. High dose of zinc can be immunosuppressive. Chronic intake of high doses of zinc can lead to copper deficiency.

**Treatment**

The treatment consists of its withdrawal and symptomatic treatment, if necessary. Further management should be as clinically indicated

5. **PHARMACOLOGICAL PROPERTIES**

**Pharmacodynamic Properties**

**5.1 Mechanism of Action/ Pharmacodynamic effects**

ZEVIT contains active substances with synergistic, prophylactic and therapeutic actions, necessary for maintenance and/or improvement of functional activities of the body.

Vitamins, their precursors and mineral (zinc) are included to treat deficiencies occurred. Many of those act as co-factors for various metabolic functions.

**Biotin**

It is involved in carbohydrate and fat metabolism.

**Folic acid**

It is essential for erythropoiesis, maturation of red blood cells and biosynthesis of the DNA.

**Vitamin B\textsubscript{1} (Thiamine Mononitrate)**
Vitamin B₁ is an essential co-enzyme in oxidative metabolism of α-ketoacids and increases the activity of acetylcholine in nerve endings.

**Vitamin B₂ (Riboflavin)**

Vitamin B₂ is an essential component in function of certain co-enzymes important for energy production taking part in numerous oxidation and reduction reactions. It has also an important role in maintaining a healthy skin.

**Pantothenic acid**

It is a precursor of co-enzyme A, necessary for energy production, involved in fatty acid metabolism, formation of acetylcholine and improvement of epithelization and wound healing. It is also necessary for folic acid and carbohydrates metabolism.

**Vitamin B₆ (Pyridoxine Hydrochloride)**

It takes part in formation of some important co-enzymes involved in protein metabolism and HEM biosynthesis. As a coenzyme it functions in metabolism of amino acids, glycogen and sphingoid bases.

**Nicotinamide**

Nicotinamide is involved in a large number of processes such as production of energy, synthesis of fatty acids, cholesterol, steroids, signal transduction and the maintenance of integrity of genome.

**Vitamin B₁₂ (Cyanocobalamin)**

It is essential for erythropoiesis, formation of myelin sheet and synthesis of the DNA.

**Vitamin C (Ascorbic acid)**

Vitamin C is an electron donor (reducing agent or antioxidant) for 11 enzymes. It has a role in hydroxylation of certain compounds. It helps in maintenance of intracellular skeleton of cartilages, bones and teeth. It is essential in maintenance of capillary wall integrity and regulation of capillary permeability. Vitamin C promotes absorption of soluble non-haem iron.

**Zinc**

Zinc is an essential component of a large number (> 300) of enzymes participating in the synthesis and degradation of carbohydrates, lipids, proteins, and nucleic acids as well as in the metabolism of other micronutrients. Zinc plays a major role in the immune system. It also acts as an antioxidant. It is important for normal growth, wound healing and sexual maturation, for crystallization and release of insulin (the pancreas of diabetic individuals contains only half of the normal quantity of zinc).

5.2 Pharmacodynamic Properties

Pharmacotherapeutic group: Multivitamins and other minerals, including combinations; ATC Code: A11AA03.

5.2 Pharmacokinetic Properties

There are no relevant data available.

6. NONCLINICAL PROPERTIES

There are no relevant data available.

7. DESCRIPTION

Capsules for oral administration.
Each capsule contains:

- Zinc Sulphate Monohydrate IP 41.4 mg (equivalent to 15 mg elemental zinc)
- Thiamine Mononitrate IP 10 mg
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Colours: Approved colours used in empty capsule shell q.s.

(Appropriate overages included for vitamins)

8. PHARMACEUTICAL PARTICULARS

List of Excipients

Paraffin liquid, gelatin triturate (cyanocobalamin), lactose, magnesium stearate and colloidal silicon dioxide.

Empty hard gelatin size ‘1’ locking type capsules with blue cap and yellow body containing gelatine, purified water, methyl paraben, propyl paraben, erythrosine, brilliant blue FCF, tartrazine, sunset yellow FCF and titanium dioxide

8.1 Incompatibilities

There are no relevant data available.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Strips of capsules in a carton.

8.4 Storage and Handling Information

There are no special requirements for use or handling of this product.

Store in a dry, well-ventilated place at a temperature not exceeding 30°C.

Store protected from light and moisture.

Do not freeze.

Keep out of reach of children.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of ZEVIT. Patients may also be informed about posology, method of administration and storage/handling information as applicable.

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.
For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited.
Registered Office
Dr. Annie Besant Road, Worli
Mumbai 400 030, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE
Manufacturing Licence number is indicated on the label and packaging.

12. DATE OF REVISION
13 -NOV-19

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Version ZEV/PI/IN/2019/02

Adapted from:
- Theragran Stress NCDS v03 dated 18 September 2018
- Theragran H NCDS v04 dated 23 November 2018
- PDR for Nutritional Supplement 2nd ed.