COBADEX FORTE CAPSULES

Vitamin B12-B Complex with Vitamin C Capsules

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains:

- Thiamine Mononitrate IP 10 mg
- Vitamin B2 IP 10 mg
- Vitamin B6 IP 3 mg
- Nicotinamide IP 100 mg
- Calcium Pantothenate IP 50 mg
- Folic Acid IP 1500 mcg
- Vitamin B12 IP 15 mcg
- Vitamin C IP 150 mg
- Biotin USP 100 mcg

Colours: Approved colours used in empty capsule shell

(Appropriate overages added)

PHARMACEUTICAL FORM

Hard Gelatin Capsules for oral administration.

CLINICAL PARTICULARS

Therapeutic Indications

COBADEX FORTE is indicated for the treatment of vitamin B-complex and vitamin C 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

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**

*COBADEX FORTE* is not recommended for pediatric use.

**Elderly**

There are no relevant data available.

**Renal Impairment**

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

**Hepatic Impairment**

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

**Contraindications**

*COBADEX FORTE* is contraindicated in hypersensitivity to any of the components.

**Special Warnings and Special 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.

**Megaloblastic anaemias**

The dose of folic acid provided is inadequate for the treatment of megaloblastic anaemias.

The development of anaemia despite prophylaxis with this medicinal product requires further investigation and appropriate therapy.

**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 B<sub>6</sub>) is associated with the development of severe peripheral neuropathies; the dose at which these occur is not established.

**Treatment preparation and monitoring**

*Cobadex Forte* should, if possible, not be given to patients with suspected vitamin B<sub>12</sub> 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.

**Interaction with Other Medicaments and Other Forms of Interaction**

**Antibiotics**

Penicillamine and antituberculous drugs (such as isoniazid) may increase the requirements for folic acid and pyridoxine (vitamin B<sub>6</sub>).

Neomycin used orally may reduce the absorption of vitamin B<sub>12</sub>.

**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 B<sub>6</sub>, vitamin B<sub>12</sub> 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**
**COBADEX FORTE** contains vitamin B₆ which reduces the effects of levodopa, but this does not occur if a dopa decarboxylase inhibitor is also given.

**Altretamine**

**COBADEX FORTE** contains vitamin B₆ which reduces the activity of altretamine.

**Anticonvulsants**

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 B₁₂ 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.

**Iron supplements**

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

**Raltitrexed**

Concomitant use of folic acid with raltitrexed should be avoided.

**Other**

Absorption of vitamin B\textsubscript{12} from the gastrointestinal tract may be reduced by aminosalicylic acid, histamine H\textsubscript{2}-antagonists, and colchicine.

**Pregnancy and Lactation**

**Fertility**

There are no relevant data available.

**Pregnancy**

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

**Lactation**

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

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

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

**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 *COBADEX FORTE*. 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
Nervous system disorders

Headache, dizziness, progression of neurological signs and symptoms of vitamin B₁₂ deficiency due to folic acid

Skin and subcutaneous tissue disorders

Photosensitivity

Renal and urinary disorders

Yellow orange discoloration to urine discoloration, hyperoxaluria

Metabolic disorders

Diabetogenic effects

Overdose

Overdose of COBADER FORTE 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.

Treatment

The treatment consists of its withdrawal and symptomatic treatment, if necessary.

Further management should be as clinically indicated or as recommended by the national poisons centre, where available.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Pharmacotherapeutic group: Vitamins, other combinations; ATC Code :A11JC.

Mechanism of Action and Pharmacodynamic Effects

COBADER FORTE contains active substances with synergistic, therapeutic actions, necessary for maintenance and/or improvement of functional activities of the body.
Vitamins, their precursors, 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 B₁ (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.

**Pharmacokinetic Properties**

There are no relevant data available.

**Clinical Studies**

There are no relevant data available.

**Preclinical Safety Data**

There are no relevant data available.

**PHARMACEUTICAL PARTICULARS**

**List of Excipients**

Paraffin liquid, magnesium stearate, colloidal silicone dioxide, starch maize, gelatin in empty hard gelatin capsule (Printed).

Colours in empty capsule shells: Tartrazine, Brilliant Blue FCF, Sunset Yellow FCF, Ponceau 4R and Titanium Dioxide.

**Incompatibilities**

There are no relevant data available.

**Shelf Life**

The expiry date is indicated on the label and packaging.

**Special Precautions for Storage**

Store at temperature not exceeding 30°C.

Protect from direct sunlight.

Keep out of reach of children.

**Nature and Specification of Container**

Aluminium strips in a carton.

**Instructions for Use/Handling**

There are no special requirements for use or handling of this product.
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Adapted from:
- Theragran Stress NCDS v 03 dated 18 September 2018
- Theragran H v 03 dated 23 August 2017
- PDR for Nutritional Supplement 2nd ed.
- Vitamins and Minerals Checklist for Local Operating Companies (LOCs) received from SERM