

# ENDOCHEK

## Composition:

ENDOCHEK is available in two strengths: ENDOCHEK 5 and ENDOCHEK 10

Each tablet of ENDOCHEK 5 contains:

Each tablet of ENDOCHEK 10 contains:

Atorvastatin	5mg
Methylcobalamin	500mcg
Folic acid	5mg
Pyridoxine	10mg

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Methylcobalamin	500mcg
Folic acid	5mg
Pyridoxine	10mg

## Pharmacology:

ENDOCHEK is a unique combination of Lipid-lowering drug like Atorvastatin and homocysteine-lowering vitamins like Methylcobalamin, folic acid and pyridoxine.

### Atorvastatin:

- Atorvastatin is a synthetic hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase inhibitor. It impedes the formation of mevalonic acid, which is the rate-limiting step in the biosynthesis of cholesterol. The reduction in intracellular cholesterol increases the number of low-density lipoprotein (LDL) receptors, thus increasing the clearance of LDL-cholesterol from plasma.
- Atorvastatin reduces plasma levels of total cholesterol, LDL-cholesterol, VLDL-cholesterol, triglycerides and apolipoprotein B, as demonstrated in a number of studies in human volunteers and patient. The greater efficacy of atorvastatin than other currently available HMG-CoA reductase inhibitors in reducing total cholesterol and LDL-cholesterol levels is believed to result from a prolonged duration of HMG-CoA reductase inhibition rather than the degree of inhibition.
- The marked reductions in triglyceride levels with atorvastatin result mainly from decreases in VLDL production, caused in part by inhibition of cholesterol synthesis.
- As well, atorvastatin possibly plays a role in the stabilization of atherosclerotic plaques by reducing the accumulation of inflammatory cells within them.
- Atorvastatin also reduced the enhanced susceptibility of LDL to oxidation, decreased cholesterol accumulation in macrophages and improved red cell deformability.

### Homocysteine-Lowering Vitamins:

**Methylcobalamin:** Methylcobalamin is one of the two-coenzyme forms of vitamin B12 (the other being adenosylcobalamin). It is a cofactor in the enzyme methionine synthase, which functions to transfer methyl groups for the regeneration of methionine from homocysteine.

## **Folic acid**

Folic acid, also known generically as folate or folacin, is a member of the B-complex family of vitamins, and works in concert with vitamin B12. Folic acid functions primarily as a methyl-group donor involved in many important body processes, including DNA synthesis. Therapeutically, folic acid is instrumental in reducing homocysteine levels and the occurrence of neural tube defects.

## **Pyridoxine:**

The standard B6 vitamin supplement is also called as pyridoxine hydrochloride. Homocysteine, an intermediate in methionine metabolism, can be re-methylated to methionine, or can also be channeled down the trans-sulfuration pathway to cysteine, which requires two P5P-dependent enzymes: cystathionine synthase and cystathionase, this process is being mediated by pyridoxine.

## **Mechanism of Homocysteine-Lowering vitamins:**

An abnormally high plasma level of homocysteine, the de-methylated derivative of the amino acid methionine, is an independent risk factor for cardiovascular disease. Elevated plasma homocysteine has been connected to increased risk of neural tube defects and other birth defects, as well as to schizophrenia, Alzheimer's disease, cognitive decline, osteoporosis, rheumatoid arthritis, kidney failure, and cancer.

The activated coenzyme form of folic acid (5-methyltetrahydrofolate) is needed for optimal homocysteine metabolism, since it acts as a methyl donor, providing a methyl group to vitamin B12. The methylated form of vitamin B12 (Methylcobalamin) subsequently transfers this methyl group to homocysteine. The result is a recycling of homocysteine to methionine, resulting in reduction in elevated plasma homocysteine.

Homocysteine can also be channeled down the trans-sulfuration pathway to cysteine, which requires two P5P-dependent enzymes: cystathionine synthase and cystathionase, this process is being mediated by pyridoxine. Homocysteine is then converted to cysteine and easily excreted out of the body.

## **Indications of Endochek:**

Fixed dose combination tablet of ENDOCHEK [Atorvastatin 5/10mg, Methylcobalamin 500mcg, Pyridoxine 10mg and Folic acid 5mg] is recommended to:

○ All patients at risk of atherosclerosis including:

- Hyperlipidemia
- Diabetes mellitus
- Hypertension
- Smoking
- Obesity
- Syndrome X

○ Patients diagnosed with CAD [Coronary Arterial Disease]

○ Patients with:

- H/o Myocardial infarction
- Angina pectoris
- Stroke
- Transient Ischemic Attack [TIA]
- Peripheral Arterial Disease [PAD]

**Contraindications:**

- The use of **ENDOCHEK** is contraindicated in patients with hypersensitivity to any of the ingredients of the formulation.

**Precautions:**

Folic acid when administered as a single agent in doses above 0.1mg daily may obscure pernicious anemia in that hematologic remission can occur while neurological manifestations remain progressive.

Unmetabolized folic acid has been shown in one study of 105 postmenopausal women (50-75yrs) to have the potential to reduce natural killer cells' cytotoxicity, which may result in an impaired immune response.

**Drug Interactions:**

**Antacid:** When atorvastatin and antacids were coadministered, plasma concentrations of atorvastatin decreased approximately 35%. However, LDL-C reduction was not altered.

**Cimetidine:** Atorvastatin plasma concentrations and LDL-C reduction were not altered by coadministration of cimetidine.

**Digoxin:** When multiple doses of atorvastatin and digoxin were coadministered, steady-state plasma digoxin concentrations increased by approximately 20%. Patients taking digoxin should be monitored appropriately.

**Erythromycin:** In healthy individuals, plasma concentrations of atorvastatin increased approximately 40% with coadministration of atorvastatin and erythromycin, a known inhibitor of cytochrome P450 3A4.

**Oral Contraceptives:** Coadministration of atorvastatin and an oral contraceptive increased AUC values for norethindrone and ethinyl estradiol by approximately 30% and 20%. These increases should be considered when selecting an oral contraceptive for a woman taking atorvastatin.

**Warfarin:** Atorvastatin had no clinically significant effect on prothrombin time when administered to patients receiving chronic warfarin treatment.

Medicines containing Pyridoxine should not be given to patients receiving the drug levodopa, because the action of levodopa is antagonized by pyridoxine. However, pyridoxine may be used concurrently in patients receiving a preparation containing both carbidopa and levodopa. Concurrent use of phenytoin and folic acid may result in decreased phenytoin effectiveness.

### **Adverse Reactions:**

**ENDOCHEK** is generally well tolerated and adverse events are rare.

Allergic sensitization has been reported following both oral and parenteral administration of folacin (folic acid). Paresthesia, somnolence, nausea and headaches have been reported with pyridoxine. Mild transient diarrhea, polycythemia vera, itching, transitory exanthema, and the feeling of swelling of the entire body has been associated with cyanocobalamin.

### **Dosage & Administration:**

The recommended dosage of **ENDOCHEK** is **one tablet daily**. The dose could be increased to 2-tablets at the advice of medical practitioner.

### **Presentation:**

**ENDOCHEK** is available in strip of 10 tablets.

### **Storage:**

**Endochek** should be stored at controlled room temperature between 15°-30° C. Protect from direct sunlight and moisture.