For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

SHELCAL-XT

1. Generic Name

Calcium, Vitamin D3, Methylcobalamin, L-Methylfolate Calcium & Pyridoxal-5-Phosphate Tablets

2. Qualitative and quantitative Composition:

Each film coated tablet contains:

Calcium Carbonate I.P……..…1250 mg

eq. to Elemental Calcium……..… 500 mg

Vitamin D_3 I.P……..….... 2000 I.U.

Mecobalamin (Methylcobalamin) I.P. ……..….... 1500 mcg

Calcium L-5 Methyltetrahydrofolate (L-Methylfolate Calcium) USP…….…… 1 mg

Pyridoxal-5-Phosphate…….. 20 mg

Colours : Red Oxide of Iron & Titanium Dioxide I.P.

The excipients used are Colloidal Silicon Dioxide, , Magnesium Stearate, , Corn Starch, Sodium Starch Glycolate, Talc Novomix brown 30184.

3. Dosage form and strength

Dosage form: Film coated tablet

Strength: Calcium Carbonate 1250 mg, Elemental Calcium 500 mg, Vitamin D3 2000 I.U, Mecobalamin 1500 mcg, L-Methylfolate Calcium 1 mg and Pyridoxal-5-Phosphate 20 mg.

4. Clinical particulars

4.1 Therapeutic indication

It is indicated for the treatment of calcium and vitamins deficiency.

4.2 Posology and method of administration

Posology

One tablet daily or as directed by the physician.

Method of administration

Tablet should be taken orally.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

Calcium:

During long-term treatment, serum calcium levels should be followed and renal function should be monitored through measurement of serum creatinine. Monitoring is especially important in elderly patients on concomitant treatment with cardiac glycosides ordiuretics 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 the treatment discontinued.

Vitamin D3:

Vitamin D3 should be used with caution in patients with impairment of renal function and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account. In patients with severe renal insufficiency, Vitamin D3 in the form of Cholecalciferol is not metabolised normally and other forms of Vitamin D3 should be used. Should be prescribed with caution to patients suffering from sarcoidosis because of the risk of increased metabolism of Vitamin D3 to its active form. These patients should be monitored with regard to the calcium content in serum and urine. Used with caution in immobilised patients with osteoporosis due to the increased risk of hypercalcaemia. Caution should be exercised while prescribing Cholecalciferol and other medicinal products containing Vitamin D3 or nutrients (such as milk). Additional doses of calcium or Vitamin D3 increase the risk of hypercalcaemia with subsequent kidney function impairment and milk-alkali syndrome; therefore they should be taken under close medical supervision. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently.

L-methylfolate calcium:

L-methylfolate calcium is not interchangeable with folic acid. Folic acid is not effective in some patients in impacting cerebral folate levels due to low rates of folic acid transport across the blood-brain barrier and/or low brain levels of the enzyme required to convert folic acid into a biological and functional form. Patients at risk for vitamin B12 deficiency should consult with their physician prior to taking L-methylfolate calcium.

Methylcobalamin:

It should be given with caution in patients suffering from folate deficiency.

The following warnings and precautions suggested with parent form – vitamin B12

- The treatment of vitamin B12 deficiency can unmask the symptoms of polycythemia vera.
- Megaloblastic anemia is sometimes corrected by treatment with vitamin B12. But this can have very serious side effects. Don't attempt vitamin B12 therapy without close supervision by your healthcare provider.
- Do not take vitamin B12 if Leber's disease, a hereditary eye disease. It can seriously harm the optic nerve, which might lead to blindness.

4.5 Drugs interactions

Calcium and vitamin D3:

Thiazide diuretics reduce the urinary excretion of calcium. Due to increased risk of hypercalcaemia, serum calcium should be regularly monitored during concomitant use of thiazide diuretics.

Systemic corticosteroids reduce calcium absorption. During concomitant use, it may be necessary to increase the dose of dosage form.

Calcium carbonate may interfere with the absorption of concomitantly administered tetracycline preparations. For this reason, tetracycline preparations should be administered at least two hours before, or four to six hours after, oral intake of calcium.

Simultaneous treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce the gastrointestinal absorption of Vitamin D3.

Hypercalcaemia may increase the toxicity of cardiac glycosides during treatment with calcium and Vitamin D3. Patients should be monitored with regard to electrocardiogram (ECG) and serum calcium levels.

If a bisphosphonate or sodium fluoride is used concomitantly, this preparation should be administered at least three hours before the intake of tablet(s) since gastrointestinal absorption may be reduced.

The efficacy of levothyroxine can be reduced by the concurrent use of calcium, due to decreased levothyroxine absorption. Administration of calcium and levothyroxine should be separated by at least four hours.

The absorption of quinolone antibiotics may be impaired if administered concomitantly with calcium. Quinolone antibiotics should be taken two hours before or after intake of calcium.

Oxalic acid (found in spinach and rhubarb) and phytic acid (found in whole cereals) may inhibit calcium absorption through formation of insoluble calcium salts. The patient should not take calcium products within two hours of eating foods high in oxalic acid and phytic acid.

Methylcobalamin

The data are unavailable for methylcobalamin drug interaction, however evidence for parent drug, vitamin B_{12} are as follows:

- Serum concentrations may be decreased by use of oral contraceptives.
- Many of these interactions are unlikely to be of clinical significance but should be taken into account when performing assays for blood concentrations.
- Parenteral chloramphenicol may attenuate the effect of vitamin B12 in anaemia.
- Folic acid, particularly in large doses, can cover up vitamin B12 deficiency, and cause serious health effects.
- Early research suggests that vitamin C supplements can destroy dietary vitamin B12. It isn't known whether this interaction is important, but to stay on the safe side, take vitamin C supplements at least 2 hours after meals.

Pyridoxal-5-phosphate

Pyridoxal-5-phosphate should not be given to patients receiving the drug levodopa, because the action of levodopa is antagonized by pyridoxal-5-phosphate. However, pyridoxal-5-phosphate may be used concurrently in patients receiving preparation containing both carbidopa and levodopa.

4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)

Pregnancy and Lactation

Calcium and vitamin D3: During pregnancy the daily intake should not exceed 1500 mg calcium and 600 IU Vitamin D3. Studies in animals have shown reproductive toxicity with high doses of Vitamin D3. In pregnant women, overdoses of calcium and Vitamin D3 should be avoided as permanent hypercalcaemia has been related to adverse effects on the developing foetus. There are no indications that Vitamin D3 at therapeutic doses is teratogenic in humans. Calcium and Vitamin D3 tablets can be used during pregnancy, in case of calcium and Vitamin D3 deficiency.

Lactation: Calcium and Vitamin D3 tablets can be used during breast-feeding. Calcium and Vitamin D3 is excreted in breast milk. This should be considered when giving additional Vitamin D3 to the child.

Methylcobalamin: Vitamin B12 is likely safe for pregnant or breast-feeding women when taken by mouth in the amounts recommended. Don’t take large amounts. The safety of larger amounts is unknown.

No data available for use of methylcobalamin in special population.

L-methylfolate calcium: L-methylfolate calcium has not been formally assigned a pregnancy risk category; there are no controlled studies in humans or animals At recommended doses, folic acid is pregnancy risk category A [adequate, well controlled studies in pregnant women have failed to demonstrate risk to the fetus] At high doses, folic acid is pregnancy risk category C [no controlled studies in humans] Because pregnant women are advised to take folic acid or prenatal vitamins that contain folic acid, it is important to ask the patient about any supplements or vitamins she may be taking and consider this when deciding whether to prescribe L-methylfolate calcium.

Breast Feeding: Some drug is found in mother's breast milk.

Pyridoxal-5-phosphate: Data on exposed pregnancies indicate no adverse effects of pyridoxine in therapeutic doses on pregnancy or the health of the foetus or newborn child, or during lactation.

Animal studies are insufficient with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development.

Caution should be exercised when prescribing to pregnant women.

4.7 Effects on ability to drive and use machines

No data is available regarding the effects on ability to drive and use machines.

4.8 Undesirable effects

Calcium and vitamin D3:

Adverse reactions are listed below, by System organ class and frequency. Frequencies are defined as: uncommon (1/1,000, to < 1/100); rare (1/10,000 to < 1/1,000) or very rare (1/10,000) Metabolism and nutrition disorders Uncommon: Hypercalcaemia and hypercalciuria. Very rare: Seen usually only in overdose: Milk-alkali syndrome Gastrointestinal disorders Rare: Constipation, dyspepsia, flatulence, nausea, abdominal pain and diarrhoea. Skin and subcutaneous disorders Rare: Pruritus, rash and urticaria.

Methylcobalamin:

Generally, methylcobalamin is well tolerated. No toxic reactions have been reported.

- Pulmonary edema and congestive heart failure early in treatment; peripheral vascular thrombosis.
- Polycythemia vera may also be seen.
- Mild transient diarrhea has been seen.
- Rarely itching; transitory exanthema.
- Other adverse effects reported with vitamin B12 are diarrhea, blood clots, itching, and serious allergic reactions

L-methylfolate calcium:

Allergic reactions have been reported following the use of oral L-methylfolate calcium.

Pyridoxal-5-phosphate:

Paresthesia, somnolence, nausea and headaches have been reported with pyridoxal-5-phosphate.

Reporting of adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Report

suspected adverse reactions via any point of contact available at www.torrentpharma.com or at email: pv@torrentpharma.com or call on 1800-120-3001.

4.9 Overdose

Calcium and vitamin D3:

Overdose can lead to hypervitaminosis D and hypercalcaemia. Symptoms of hypercalcaemia may include anorexia, thirst, nausea, vomiting, constipation, abdominal pain, muscle weakness, fatigue, mental disturbances, polydipsia, polyuria, bone pain, nephrocalcinosis, nephrolithiasis and in severe cases, cardiac arrhythmias. Extreme hypercalcaemia may result in coma and death. Persistently high calcium levels may lead to irreversible renal damage and soft tissue calcification. Milk-alkali syndrome (frequent urge to urinate; continuing headache; continuing loss of appetite; nausea or vomiting; unusual tiredness or weakness; hypercalcaemia, alkalosis and renal impairment). The milk-alkali syndrome of hypercalcaemia, alkalosis and renal impairment still occur in patients who ingest large amounts of calcium and absorbable alkali; it is not uncommon as a cause of hypercalcaemia requiring hospitalisation. The syndrome has also been reported in a patient taking recommended doses of antacids containing discomfort, and in a pregnant woman taking high, but not grossly excessive, doses of calcium (about 3 g of elemental calcium daily). Metastatic calcification can develop. Treatment of hypercalcaemia The treatment with Calcium and Vitamin D3 must be discontinued. Treatment with thiazide diuretics, lithium, vitamin A and cardiac glycosides must also be discontinued. Treatment is rehydration, and, according to severity of hypercalcaemia, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids should be considered. Serum electrolytes, renal function and diuresis must be monitored. In severe cases, ECG and CVP should be followed.

Methylcobalamine, L-methylfolate calcium, Pyridoxal-5-Phosphate

No information available for overdose.

5. Pharmacological properties

5.1.Mechanism of Action

Calcium Carbonate:

It prevents or treats negative Ca balance. It is essential for normal functioning of nerves, cells, muscle and bone.

Vitamin D3:

Vitamin D3 increases the intestinal absorption of calcium and phosphate. It also counteracts the increase of parathyroid hormones (PTH) which are caused by calcium deficiency, and which causes increased bone resorption.

Mecobalamin:

Mecobalamin is well transported to nerve cell organelles than cyanocobalamin and plays the role of coenzyme in the synthesis of methionine from homocysteine.

L-Methylfolate Calcium:

Folic acid is a precursor of tetrahydrofolic acid, which is involved as a cofactor for transformylation reactions. These reactions are involved in the biosynthesis of thymidylates and purines of nucleic acids.

Pyridoxal-5-Phosphate:

Pyridoxal Phosphate is a coenzyme of many enzymatic reactions. It is the active form of vitamin B6 which comprises three natural organic compounds, pyridoxal, pyridoxamine and

pyridoxine. Pyridoxal phosphate acts as a coenzyme in all transamination reactions, and in some decarboxylation and deamination reactions of amino acids.

5.2.Pharmacodynamic properties

Calcium Carbonate:

Dietary supplement: Prevents or treats negative Ca balance; oral Ca supplements may protect against renal calculi formation by chelating with oxalate in gut and preventing its absorption

Phosphate binder: Binds with dietary phosphate to form insoluble calcium phosphate, which is excreted in feces.

Vitamin D3:

The in vivo synthesis of the predominant two biologically active metabolites of vitamin D occurs in two steps. The first hydroxylation of vitamin D3 cholecalciferol (or D2) occurs in the liver to yield 25-hydroxyvitamin D while the second hydroxylation happens in the kidneys to give 1, 25-dihydroxyvitamin D.

Mecobalamin:

Mecobalamin is the one and only homologue of Vitamin B12 found in the brain that participates in transmethylation. Mecobalamin is well transported to nerve cell organelles than cyanocobalamin and plays the role of coenzyme in the synthesis of methionine from homocysteine. It is also involved in the synthesis of thymidine from deoxyuridine thus promoting nucleic acid protein synthesis.

L-Methylfolate Calcium:

L-Methylfolate Calcium is the primary biologically active isomer of folic acid and the primary form of folate in circulation. Folic acid is a precursor of tetrahydrofolic acid, which is involved as a cofactor for transformylation reactions. These reactions are involved in the biosynthesis of thymidylates and purines of nucleic acids.

Pyridoxal-5-Phosphate:

Pyridoxal Phosphate is a coenzyme of many enzymatic reactions. It is the active form of vitamin B6 which comprises three natural organic compounds, pyridoxal, pyridoxamine and pyridoxine. Pyridoxal phosphate acts as a coenzyme in all transamination reactions, and in some decarboxylation and deamination reactions of amino acids. The aldehyde group of pyridoxal phosphate forms a Schiff-base linkage with the epsilon-amino group of a specific lysine group of the aminotransferase enzyme. The alpha-amino group of the amino acid substrate displaces the epsilon-amino group of the active-site lysine residue. The resulting aldimine becomes deprotonated to become a quinoid intermediate, which in turn accepts a proton at a different position to become a ketimine. The resulting ketimine is hydrolysed so that the amino group remains on the protein complex.

5.3.Pharmacokinetic properties

Calcium Carbonate:

Absorption: The amount of calcium absorbed through the gastrointestinal tract is approximately 30% of the swallowed dose.

Distribution and metabolism: 99% of the calcium in the body is concentrated in the hard structure of bones and teeth. The remaining 1% is present in the intra - and extracellular fluids. About 50% of the total blood-calcium content is in the physiologically active ionised form with approximately 10% being complexed to citrate, phosphate or other anions, the remaining 40% being bound to proteins, principally albumin.

Elimination: Calcium is eliminated through faeces, urine and sweat. Renal excretion depends on glomerular filtration and calcium tubular reabsorption.

Vitamin D3:

Absorption: Vitamin D3 is easily absorbed in the small intestine.

Distribution and metabolism: Vitamin D3 and its metabolites circulate in the blood bound to a specific globulin. Vitamin D3 is converted in the liver by hydroxylation to the active form 25-hydroxycholecalciferol. It is then further converted in the kidneys to 1,25 hydroxycholecalciferol; 1,25 hydroxycholecalciferol is the metabolite responsible for increasing calcium absorption. Vitamin D3 which is not metabolised is stored in adipose and muscle tissues.

Elimination: Vitamin D3 is excreted in faeces and urine.

Methylcobalamin:

It binds to intrinsic factor; a glycoprotein secreted by the gastric mucosa, and is then actively absorbed from the gastrointestinal tract. Absorption is impaired in patients with an absence of intrinsic factor, with a malabsorption syndrome or with disease or abnormality of the gut, or after gastrectomy. Absorption from the gastrointestinal tract can also occur by passive diffusion; little of the vitamin present in food is absorbed in this manner although the process becomes increasingly important with larger amounts such as those used therapeutically.

It is extensively bound to specific plasma proteins called transcobalamins; Transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. A parent form -vitamin B12 is stored in the liver, excreted in the bile, and undergoes extensive enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours; urinary excretion, however, accounts for only a small fraction in the reduction of total body stores acquired by dietary means. Vitamin B12 diffuses across the placenta and also appears in breast milk.

L-methylfolate calcium

Absorption and Elimination: L-methylfolate calcium is a water-soluble molecule which is primarily excreted via the kidneys. Reportedly, in a study of subjects with coronary artery disease (n=21), peak plasma levels were reached in 1-3 hours following oral/parenteral administration. Peak concentrations of L-methylfolate calcium were found to be more than seven times higher than folic acid (129 ng/ml vs. 14.1 ng/ml) following oral/parenteral administration. The mean elimination half-life is approximately 3 hours for L-methylfolate calcium after the administration of 5mg of oral D,Lmethylfolate. The mean values for Cmax, Tmax, and AUC_{0-12} were 129 ng/ml, 1.3 hr., and 383 respectively.

Distribution: Red blood cells (RBCs) appear to be the storage depot for folate, as RBC levels remain elevated for periods in excess of 40 days following discontinuation of supplementation. Plasma protein binding studies showed that L-methylfolate calcium is 56% bound to plasma proteins.

6. Nonclinical properties

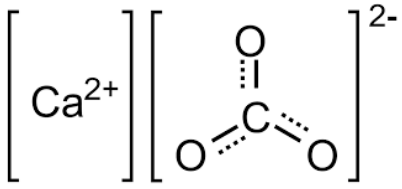
6.1. Animal Toxicology or Pharmacology

No data on animal studies of safety pharmacology available.

7.Description

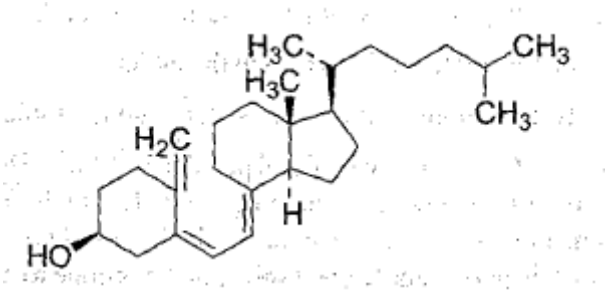
Calcium Carbonate:

Calcium Carbonate is a fine, white, microcrystalline powder .It is slightly soluble in water containing carbon dioxide or any ammonium salt, practically insoluble in water and in ethanol (95 per cent). It is soluble with effervescence in dilute acids. Calcium Carbonate empirical formula is $CaCO_3$, and its molecular weight is 100.1 g/mol. The chemical structural formula is.



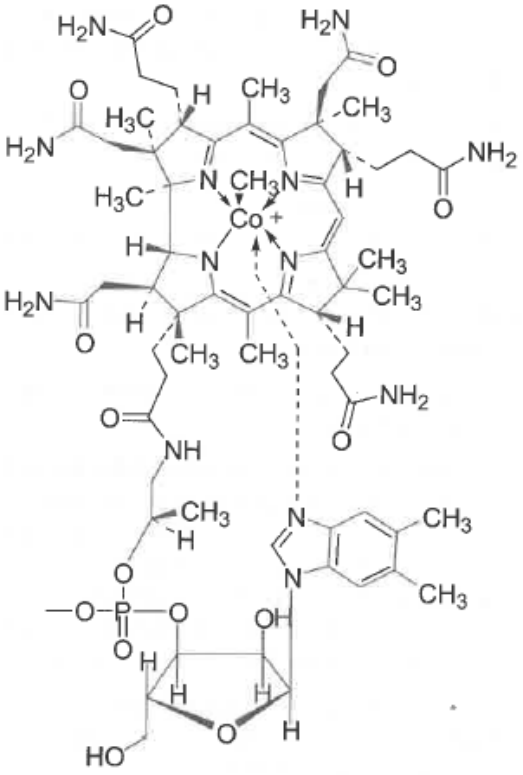
Vitamin D3:

Cholecalciferol is a white or almost white crystals. It is sensitive to air, heat and light. A reversible isomerization to precholecalciferol may occur in solution, depending on temperature and time. It is freely soluble in ethanol (95 per cent), in acetone, in chloroform and in ether, practically insoluble in water. It is soluble in fixed oils. Solutions in volatile solvents are unstable and should be used immediately. Cholecalciferol is (5Z, 7E)-(3S)-9,10-secocholesta-5,7,10(19)-triene-3-ol. The empirical formula is $C_{27}H_{44}O$ and its molecular weight is 384.6 g/mol. The chemical structural formula is.



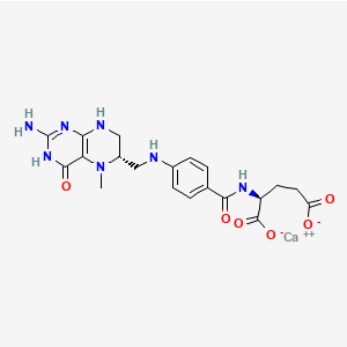
Methylcobalamin:

Methylcobalamin is a dark red crystalline powder. Methylcobalamin is Coα-[α-(5,6-dimethyl-1H-benzoimidazole-1-yl)]-Co*β*-Methylcobamide. The empirical formula is $C_{63}H_{91}CoN_{13}O_{14}P$ and its molecular weight is 1344.4 g/mol. It is sparingly soluble in water, slightly soluble in ethanol and practically insoluble in acetonitrile. The chemical structural formula is.



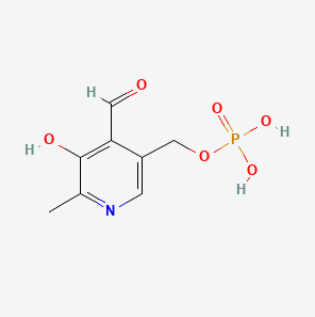
L-Methylfolate Calcium:

L-Methylfolate Calcium is calcium;(2S)-2-[[4-[[(6S)-2-amino-5-methyl-4-oxo-3,6,7,8-tetrahydropteridin-6-yl] methylamino]benzoyl] amino]pentanedioate. The empirical formula is $C_{20}H_{23}CaN_7O_6$ and its molecular weight is 497.5 g/mol. The chemical structural formula is.



Pyridoxal-5-Phosphate:

Pyridoxal-5-Phosphate is (4-formyl-5-hydroxy-6-methylpyridin-3-yl) methyl dihydrogen phosphate. The empirical formula is $C_8H_{10}NO_6P$ and its molecular weight is 247.14 g/mol. The chemical structural formula is.



SHELCAL XT

Calcium, Vitamin D3, Methylcobalamin, L-Methylfolate Calcium & Pyridoxal-5-Phosphate are Reddish Brown colored , Capsule shaped, biconvex, film coated tablets with break line on one side and plain on other side.

The excipients used are Colloidal Silicon Dioxide, , Magnesium Stearate, , Corn Starch, Sodium Starch Glycolate, Talc ,Novomix brown 30184. .

8. Pharmaceutical particulars

8.1 Incompatibilities

Not applicable

8.2 Shelf-life

Do not use later than date of expiry.

8.3 Packaging information

SHELCAL-XT is available in pack of 15 Tablets.

8.4 Storage and handing instructions

Store protected from light & moisture, at a temperature not exceeding 30°C.

Keep all medicine out of reach of children.

9. Patient Counselling Information

Ask the patients to inform the treating physicians in case of any of the below:

- Have any allergies
- Have kidney or liver problems
- Are pregnant or plan to become pregnant
- Are breastfeeding or plan to breastfeed
- Have any serious illness
- Are taking any medicines (prescription, over-the-counter, vitamins, or herbal products)

10. Details of manufacturer

Torrent Pharmaceuticals Ltd.

32 No. Middle Camp NH-10,

East District, Gangtok, Sikkim-737 135.

11. Details of permission or licence number with date

M/564/2010 dated on 27.08.2024

12. Date of revision

JUN 2026

MARKETED BY

TORRENT PHARMACEUTICALS LTD.

IN/SHELCAL-XT (1250 mg +500 mg +2000 I.U.+1500mcg+1mg+20mg)/JUN 2026/03/PI