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

SHELCAL MOM

1. Generic Name:

Calcium Carbonate, Pyridoxal-5-Phosphate, Folic Acid, Vitamin D_3, Cyanocobalamin with Docosahexaenoic Acid (DHA) Tablets

2. Qualitative and quantitative composition:

Each serving per film coated tablet contains:		% RDA
Calcium carbonate equivalent to Elemental Calcium	500 mg	42%*
Docosahexaenoic Acid (DHA) 10%	150 mg	-
Folic Acid	294 mcg	100%*
Vitamin D_3 (Stabilized)	400 IU	100%*
Cyanocobalamin (B_{12})	1.2 mcg	100%*
Pyridoxal-5'-Phosphate	2.5 mg	100%*

* % RDA considered for pregnant women

Appropriate overages of vitamins added to compensate the loss on storage.

Ingredients: Calcium Carbonate, Docosahexaenoic Acid, Microcrystalline Cellulose (INS 460(i)), Crospovidone (INS 1202), Hydroxypropyl Cellulose (INS 463), Croscarmellose Sodium (INS 466), Hydroxypropyl methyl cellulose (INS 464), Talc (INS 553(iii)), Vitamin D3, Colloidal Silicon Dioxide (INS 551), Magnesium Stearate, Polyethylene glycol (INS 1521), Pyridoxal-5-Phosphate, Sodium Methyl Paraben, Ethyl Cellulose (INS 462), Folic Acid, Butylated Hydroxy Anisole (INS 320), Butylated Hydroxy Toluene (INS 321), Cyanocobalamin and Propyl Paraben Sodium.

Contains Permitted Natural Colours (Titanium Dioxide (INS 171), Red Iron Oxide (NS 172(ii)) and Added Artificial Flavouring Substance (Vanilla Flavour).

3. Dosage form and strength:

Dosage form: Film coated tablets

Strength: 500 mg, 2.5 mg, 294 mcg, 400 IU, 1.2 mcg, 150 mg

4. Clinical particulars:

4.1 Therapeutic indication:

Shelcal MOM is indicated in the management of associated deficiencies of Calcium, Folic Acid, Cyanocobalamin and vitamin D_3 in pregnancy.

4.2 Posology and method of administration:

One tablet a day or as directed by the Healthcare Professional

4.3 Contraindications:

- Hypersensitivity to the active substances or to any of the excipients.

- Diseases and/or conditions resulting in in hypercalcaemia and/or hypercalciuria (e.g. myeloma, bone metastases, primary hyperparathyroidism).
- Nephrolithiasis
- Renal failure
- Hypervitaminosis D
- Sarcoidosis
- Vitamin D overdosage
- Long-term therapy is contraindicated in any patient with untreated cobalamin deficiency. This can be untreated pernicious anaemia or other cause of cobalamin deficiency, including lifelong vegetarians. In elderly people, a cobalamin absorption test should be done before long-term therapy. Folate given to such patients for 3 months or longer has precipitated cobalamin neuropathy. No harm results from short courses of folate.
- Should never be given alone in the treatment of Addisonian pernicious anaemia and other vitamin B_{12} deficiency states because it may precipitate the onset of subacute combined degeneration of the spinal cord.
- Should not be used in malignant disease unless megaloblastic anaemia owing to folate deficiency is an important complication.

4.4 Special warnings and precautions for use:

Calcium Carbonate
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 or diuretics 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.

Docosahexaenoic Acid (DHA)
None Stated

Vitamin D_3
Vitamin D_3 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 D_3 in the form of Cholecalciferol is not metabolised normally and other forms of Vitamin D_3 should be used. Should be prescribed with caution to patients suffering from sarcoidosis because of the risk of increased metabolism of Vitamin D_3 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 D_3 or nutrients (such as milk). Additional doses of calcium or Vitamin D_3 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.

Folic acid
Patients with vitamin B_{12} deficiency should not be treated with folic acid unless administered with adequate amounts of hydroxocobalamin, as it can mask the condition but the subacute irreversible damage to the nervous system will continue. The deficiency can be due to undiagnosed megaloblastic anaemia including in infancy, pernicious anaemia or macrocytic

anaemia of unknown aethiology or other cause of cobalamin deficiency, including lifelong vegetarians. Therefore, a full clinical diagnosis should be made before initiating treatment. Folate should not be routinely used in patients receiving coronary stents. Caution should be exercised when administering folic acid to patients who may have folate dependent tumours. Folic acid is removed by haemodialysis. Patients with rare hereditary problems of galactose intolerance, the lapp lactase deficiency or glucose – galactose malabsorption should not take this medicine.

Cyanocobalamin
Patients with early Leber's disease (hereditary optic nerve atrophy) who were treated with vitamin B_{12} suffered severe and swift optic atrophy. Hypokalemia and sudden death may occur in severe megaloblastic anemia which is treated intensely with vitamin B_{12}. Folic acid is not a substitute for vitamin B_{12} although it may improve vitamin B_{12}-deficient megaloblastic anemia. Exclusive use of folic acid in treating vitamin B_{12}- deficient megaloblastic anemia could result in progressive and irreversible neurologic damage. Blunted or impeded therapeutic response to vitamin B_{12} may be due to such conditions as infection, uremia and drugs having bone marrow suppressant properties such as chloramphenicol, and concurrent iron or folic acid deficiency. Doses of vitamin B_{12} exceeding 10 mcg daily may produce hematologic response in patients with folate deficiency. Indiscriminate administration may mask the true diagnosis. The validity of diagnostic vitamin B_{12} or folic acid blood assays could be compromised by medications, and this should be considered before relying on such tests for therapy. Vitamin B_{12} is not a substitute for folic acid and since it might improve folic acid deficient megaloblastic anemia, indiscriminate use of vitamin B_{12} could mask the true diagnosis.
Hypokalemia and thrombocytosis could occur upon conversion of severe megaloblastic to normal erythropoiesis with vitamin B_{12} therapy. Therefore, serum potassium levels and the platelet count should be monitored carefully during therapy. Vitamin B_{12} deficiency may suppress the signs of polycythemia vera. Treatment with vitamin B_{12} may unmask this condition.

Pyridoxal 5'-Phosphate
None Stated

4.5 Drug-Interaction:

Calcium Carbonate 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 D_3. 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.

Docosahexaenoic Acid (DHA)
None stated

Folic acid
Caution should be exercised when administering folic acid to epileptics. It may cause reduction in the plasma concentrations of phenytoin, primidone, phenobarbital, sodium valproate, carbamazepine and the barbiturates.

Trimethoprim or sulfonamides, alone or in combination as co-trimoxazole, may reduce the effect of folic acid and this may be serious in patients with megaloblastic anaemia. Sulphasalazine and triamterene can reduce the absorption of folic acid.

Folic acid may interfere with the toxic and therapeutic effects of methotrexate.

Methotrexate and trimethoprim are specific anti-folates and the folate deficiency caused by their prolonged use cannot be treated by Folic Acid Tablets. Folinic acid should be used.

Folate supplements enhance the efficacy of lithium therapy. Nitrous oxide anaesthesia may cause an acute folic acid deficiency. Both ethanol and aspirin increase folic elimination.

Concurrent administration with cholestyramine may interfere with folic acid absorption. Patients on prolonged cholestyramine therapy should take folic acid 1 hour before or 4 to 6 hours after receiving cholestyramine.

Antibiotics may interfere with the microbiological assay for serum and erythrocyte folic acid concentrations and may cause falsely low results.

Fluorouracil toxicity may occur in patients taking folic acid and this combination should be avoided.

Edible clay or antacids containing aluminium or magnesium may reduce folic acid absorption. Patients should be advised to take antacids at least two hours after administration of folic acid. Folic acid may reduce intestinal absorption of zinc (of particular importance in pregnancy).

Cyanocobalamin
Absorption may be reduced by Para-aminosalicylic acid, colchinine, biguanides, neomycin, cholestyramine, potassium chloride, methyldopa, and cimetidine.

Patients treated with chloramphenicol may respond poorly to this medicine.

Serum levels of this medicine may be lowered by oral contraceptives. These interactions are unlikely to have clinical significance.

Anti-metabolities and most antibiotics invalidate vitamins B12 assays by microbiological

techniques.

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 a preparation containing both carbidopa and levodopa.

4.6 Use in special populations

Calcium Carbonate and vitamin D_3
Pregnancy
During pregnancy the daily intake should not exceed 1500 mg calcium and 600 IU Vitamin D_3. Studies reported in animals have shown reproductive toxicity with high doses of Vitamin D_3. In pregnant women, overdoses of calcium and Vitamin D_3 should be avoided as permanent hypercalcaemia has been related to adverse effects on the developing foetus. There are no indications that Vitamin D_3 at therapeutic doses is teratogenic in humans. Calcium and Vitamin D3 tablets can be used during pregnancy, in case of a calcium and Vitamin D_3 deficiency.

Lactation
Calcium and Vitamin D_3 tablets can be used during breast-feeding. Calcium and Vitamin D_3 pass into breast milk. This should be considered when giving additional Vitamin D3 to the child.

Docosahexaenoic Acid (DHA)
None Stated

Folic acid
Pregnancy
There are no known hazards to the use of folic acid in pregnancy, supplements of folic acid are often beneficial.

Non-drug-induced folic acid deficiency, or abnormal folate metabolism, is related to the occurrence of birth defects and some neural tube defects. Interference with folic acid metabolism or folate deficiency induced by drugs such as anticonvulsants and some antineoplastics early in pregnancy results in congenital anomalies. Lack of the vitamin or its metabolites may also be responsible for some cases of spontaneous abortion and intrauterine growth retardation.

Imbalance in folate requiring trophoblast cells may also lead to detachment of the placenta.

Very high doses of folic acid have been shown to cause foetal abnormalities in rats; however, harmful effects in the human foetus, mother or the pregnancy have not been reported following ingestion of folic acid.

Lactation
Folic acid is actively excreted in human breast milk. Accumulation of folate in milk takes precedence over maternal folate needs. Levels of folic acid are relatively low in colostrum but as lactation proceeds, concentrations of the vitamin rise. No adverse effects have been observed in breast fed infants whose mothers were receiving folic acid.

Cyanocobalamin
Pregnancy
Animal reproduction studies have not been conducted with vitamin B_{12}. It is also not known whether vitamin B_{12} can cause fetal harm when administered to a pregnant woman or can affect

reproduction capacity. Adequate and well-controlled studies have not been done in pregnant women. However, vitamin B_{12} is an essential vitamin and requirements are increased during pregnancy.

Breast-feeding
Vitamin B_{12} appears in the milk of nursing mothers in concentrations which approximate the mother's vitamin B_{12} blood level.

Pyridoxal-5-phosphate
Pyridoxal-5-phosphate is the active form of Pyridoxine.

Pregnancy and lactation
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 D_3
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.

Docosahexaenoic Acid (DHA)
Adverse effects include anemia, cough, CNS depression, drowsiness, headache, heart damage, lassitude (weakness, exhaustion), liver damage, narcosis, reproductive effects and teratogenic effects.

Folic acid
Folic acid is generally well tolerated although the following side effects have been reported:

Gastrointestinal disorders Rare (≥1/10,000 to <1/1,000)	Anorexia, nausea, abdominal distension and flatulence
Immune system disorders Rare (≥1/10,000 to <1/1,000) Not known	 Allergic reactions, comprising erythema, rash, pruritus, urticaria, dyspnoea, and anaphylactic reactions (including shock). Anaphylactic reaction
Blood and lymphatic system disorders	Folic acid may worsen the symptoms of co-existing vitamin B_{12} deficiency and should

	never be used to treat anaemia without a full investigation of the cause.

Cyanocobalamin
Sensitisation to this medicine is rare, but may present as an itching exanthema, and exceptionally as anaphylactic shock.
Acne form and bullous eruptions have been reported rarely.
Patients who have become sensitized to this medicine by injection are often able to tolerate the oral route without trouble.

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

Reporting of side effects:

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:
http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting.

4.9 Overdose:

Calcium and vitamin D_3
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 D_3 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.

Docosahexaenoic Acid (DHA)
None Stated.

Folic acid
No cases of acute overdosage appear to have been reported, but even extremely high doses are unlikely to cause harm to patients.

No special procedure or antidote are likely to be needed, treat symptomatically.

Cyanocobalamin
Overdosage is unlikely to require treatment.

Pyridoxal-5-Phosphate
Evidences are not available for overdose.

5. Pharmacological properties:

5.1 Mechanism of Action:

Calcium is a mineral that is present naturally in the food. It is necessary for many normal functions of body mainly, bone formation and maintenance. Vitamin D, in addition to increasing intestinal calcium absorption, reducing parathyroid hormone levels and improving the amount and quality of bone, has a beneficial vascular effect. DHA acts as a ligand at peroxisome proliferator-activated receptor (PPAR) gamma and alpha that regulate lipid signalling molecule-mediated transduction pathways and modulate inflammation. As a natural ligand, DHA induces a protective effect in retinal tissues by activating retinoid x receptors and subsequent ERK/MAPK signaling pathway in photoreceptors to promote their survival and differentiation, stimulating the expression of antiapoptotic proteins such as Bcl-2 and preserving mitochondrial membrane potential. Folic acid is a member of the vitamin B group. Folic acid is reduced in the body to tetrahydrofolate, which is a co-enzyme for various metabolic processes including the synthesis of purine and pyrimidine nucleotides, and hence in the synthesis of DNA; it is also involved in the formation and utilisation of formate. cyanocobalamin vitamin B_{12}, which is used for the treatment of pernicious anaemia, and nutritional deficiencies of vitamin B_{12} which results in macrocytic anaemia. Pyridoxal phosphate acts as a coenzyme in all transamination reactions, and in some oxylation and deamination reactions of amino acids.

5.2 Pharmacodynamic properties:

Calcium Carbonate
Calcium is the most abundant mineral in the human body and is essential for maintaining the functional integrity of nervous and musculoskeletal systems as well as cell membrane and capillary permeability. The majority (99%) of the body calcium is contained in bone with the remainder equally disturbed between intra- and extra cellular fluids. Calcium is an activator in many enzymatic reactions and is necessary for nerve impulse transmission, renal function, respiration and blood coagulation.

Docosahexaenoic Acid (DHA)
DHA in the central nervous system is found in the phospholipid bilayers where it modulates the physical environment and increase the free volume within the membrane bilayer. It influences the G-protein coupled receptor activity and affects transmembrane transport and cell interaction with the exterior world. It is also reported to promote apoptosis, neuronal differentiation and ion channel activity. Like other polyunsaturated fatty acids, DHA acts as a ligand at PPARs that plays an anti-inflammatory effect and regulate inflammatory gene expression and NFκB activation. DHA also gives rise to resolvins and related compounds (e.g., protectins) through pathways involving cyclooxygenase and lipoxygenase enzymes to resolve the inflammatory responses.

Folic Acid
Folic acid is a member of the vitamin B group. Folic acid is reduced in the body to tetrahydrofolate, which is a co-enzyme for various metabolic processes including the synthesis

of purine and pyrimidine nucleotides, and hence in the synthesis of DNA; it is involved in the formation and utilisation of formate.

Deficiency of folic acid leads to megaloblastic anaemia. Deficiency may result from a diminished intake, as in malnutrition, from malabsorption, or from the concomitant use of anticonvulsants or dihydrofolate reductase inhibitors such as pyrimethamine, trimethoprim, or methotrexate.

Vitamin D_3
Vitamin D_3 increases the intestinal absorption of calcium. Administration of calcium and Vitamin D_3 counteracts the increase of parathyroid hormone (PTH) which is caused by calcium deficiency and which causes increased bone reabsorption.

Cyanocobalamin
Vitamin B_{12} is essential for growth, cell reproduction, hematopoiesis, and nucleoprotein and myelin synthesis. Rapidly dividing cells (e.g., epithelial cells, bone marrow, myeloid cells) have the greatest requirement for vitamin B_{12}. In tissues, vitamin B_{12} is essential for the conversion of methylmalonate to succinate and for the synthesis of methionine from homocysteine. In the absence of vitamin B_{12}, tetrahydrofolate cannot be regenerated from 5-methyl tetrahydrofolate, and functional folate deficiency occurs. Vitamin B_{12} also may be involved in sulfhydrylactivated enzyme systems associated with fat and carbohydrate metabolism and protein synthesis. An elevated serum homocysteine concentration appears to be a risk factor for osteoporotic fractures in older men and women. Treatment with vitamin B_{12} and folate can reduce plasma homocysteine concentrations. In a placebo-controlled study of patients with hemiplegia following stroke (and at increased risk of hip fracture), those given folate and vitamin B_{12} were found to have a significantly reduced risk of hip fracture despite a lack of effect on bone mineral density. Vitamin B_{12} status has been associated with bone health in a number of studies and it was suggested that the observed effects on fracture might be due to increased concentrations of vitamin B_{12} rather than the lowering of plasma homocysteine.

Pyridoxal-5-Phosphate

Pyridoxal Phosphate is the active form of vitamin B_6 and a coenzyme for many pyridoxal phosphate (PLP)-dependent enzymes. PLP is involved in numerous enzymatic transamination, decarboxylation and deamination reactions; it is necessary for the synthesis of amino acids and amino acid metabolites, and for the synthesis and/or catabolism of certain neurotransmitters, including the conversion of glutamate into gamma-aminobutyric acid (GABA) and levodopa into dopamine. PLP can be used as a dietary supplement in cases of vitamin B_6 deficiency. Reduced levels of PLP in the brain can cause neurological dysfunction.

5.3 Pharmacokinetic properties:

Calcium carbonate
Calcium is actively absorbed, mainly in the duodenum and proximal jejunum. Calcium must be in a soluble, ionized from to be absorbed. Factors such as an acidic intestinal pH, the presence of the Vitamin D, and pregnancy and lactation tend to favour calcium absorption. However, absorption may be impeded in the elderly, or by a deficiency of parathyroid hormone, calcium or Vitamin D, the presence of anions or fatty acids which may precipitate or complex with

calcium, or in certain disease states such as achlorhydria, renal oateodystrophy, steatorrhea or ureinia.
Once absorbed into the bloodstream, most calcium is rapidly incorporated into skeletal muscle; the remainder is equally distributed between intra- and extra cellular fluids. Normal total serum calcium concentrations range from 2.2 to 2.6 mmol/L, although only the ionized fraction is physiologically active. Of the total serum calcium, 50% is ionized, 5% is complexed with anions such as phosphates or citrates and 45% is protein bound. Hyperproteinemia is associated with an increase in total scrum calcium; hypoprotienemia has the opposite effect. Acidosis favors an increase in ionic calcium concentration, while alkalosis leads to a decrease in the ionized fraction. CSF calcium concentrations tend to be similar to the serum concentration of ionized calcium, i.e., approximately 50% of total serum calcium. Calcium crosses the placenta, reaching higher levels in fatal blood than in the mother. Calcium is excreted in breast milk.
Calcium is excreted mainly in the faces, either as a result of passing through the gut unabsorbed or through biliary or pancreatic secretion into gut lumen. Very small amounts of calcium are excreted in the urine as most filtered calcium is reabsorbed. Urinary excretion of calcium is promoted by growth hormone, Vitamin D, thiazide diuretics or a decrease in ionizes calcium concentration tend to decrease the amount of calcium excreted in the urine, Calcium is also excreted in sweat.

Docosahexaenoic Acid (DHA)
DHA is hydrolyzed from the intestines and delivered through the lymphatic circulation. Plasma DHA concentrations increase in a dose-dependent and saturable manner. DHA is the most abundant n−3 fatty acid in membranes and is present in all organs. It is also the most variable among organs and is particularly abundant in neural tissue, such as brain and retina, where it is several hundred-fold more abundant than EPA. DHA can be metabolized into DHA-derived specialized pro-resolving mediators (SPMs), DHA epoxides, electrophilic oxo-derivatives (EFOX) of DHA, neuroprostanes, ethanolamines, acylglycerols, docosahexaenoyl amides of amino acids or neurotransmitters, and branched DHA esters of hydroxy fatty acids, among others. It is converted to 17-hydroperoxy-DHA derivatives via COX-2 and 15-LOX and 5-LOX activity. These derivatives are further converted into D-series resolvins and protectins with potent anti-inflammatory potential and potent neuroprotective effect. DHA may also be metabolized to 19, 20-epoxydocosapentaenoic acids (EDPs) and isomers via CYP2C9 activity. Epoxy metabolites are reported to mediate anti-tumor activity by inhibiting angiogenesis, tumor growth, and metastasis.

Folic Acid
Folic acid is absorbed mainly from the proximal part of the small intestine. Dietary folates are stated to have about half the bioavailability of crystalline folic acid. Folate polyglutamates are considered to be deconjugated to monoglutamates during absorption. Folic acid given therapeutically enters the portal circulation largely unchanged, since it is a poor substrate for reduction by dihydrofolate reductases. Folic acid rapidly appears in the blood, where it is extensively bound to plasma proteins. The principal storage site of folate is in the liver; it is also actively concentrated in the CSF. The amounts of folic acid absorbed from normal diets are rapidly distributed in body tissues and about 4 to 5 ug is excreted in the urine daily. There is an enterohepatic circulation for folate. When larger amounts are absorbed a high proportion is metabolised in the liver to other active forms of folate and a proportion is stored as reduced and methylated folate. Larger amounts of folate are rapidly excreted in the urine. Folic acid is

removed by haemodialysis. Folate is distributed into breast milk.

Cyanocobalamin
Vitamin B_{12} substances bind to intrinsic factor; a glycoprotein secreted by the gastric mucosa, and are 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. Gastrointestinal absorption of vitamin B_{12} depends on the presence of sufficient intrinsic factor and calcium ions. Intrinsic factor deficiency causes pernicious anemia, which may be associated with sub-acute combined degeneration of the spinal cord. Prompt parenteral administration of vitamin B_{12} prevents progression of neurologic damage.
The average diet supplies about 4 to 15 mcg/day of vitamin B_{12} in a protein-bound form that is available for absorption after normal digestion. Vitamin B_{12} is not present in foods of plant origin, but is abundant in foods of animal origin. In people with normal absorption, deficiencies have been reported only in strict vegetarians who consume no products of animal origin (including no milk products or eggs). Vitamin B_{12} is bound to intrinsic factor during transit through the stomach; separation occurs in the terminal ileum in the presence of calcium, and vitamin B_{12} enters the mucosal cell for absorption. It is then transported by the transcobalamin binding proteins. A small amount (approximately 1% of the total amount ingested) is absorbed by simple diffusion, but this mechanism is adequate only with very large doses. Oral absorption is considered too undependable to rely on in patients with pernicious anemia or other conditions resulting in malabsorption of vitamin B_{12}. Colchicine, para-aminosalicylic acid, and heavy alcohol intake for longer than 2 weeks may produce malabsorption of vitamin B_{12}. The absorption of cobalamins from the gut is dependent upon the glycoprotein intrinsic factor. Cobalamins are transported rapidly into the blood bound to protein, known as transcobalamins. Cobalamins are stored in the liver and excreted in the bile. They are known to cross the placenta.

Pyridoxal -5-Phosphate
Pyridoxal-5-phosphate (PLP) is the active form of vitamin B_6 and is used as the prosthetic group for many of the enzymes where this vitamin is involved. PLP is readily absorbed by the intestine by a process which is preceded by dephosphorylation to form pyridoxal. The phosphate group is regained during passage through the intestine. Pyridoxine, the parent compound of PLP and the most frequently used form of vitamin B6, requires reduction and phosphorylation before becoming biologically active.

6. Nonclinical properties:

6.1 Animal Toxicology or Pharmacology

None stated.

7. Description:

Calcium Carbonate, Pyridoxal-5-Phosphate, Folic Acid, Vitamin D_3, Cyanocobalamin with Docosahexaenoic Acid (DHA) Tablets are brown coloured, oval shaped, biconvex, film coated tablets, breakline on both sides. The excipients used are Calcium Carbonate, Docosahexaenoic Acid, Microcrystalline Cellulose (INS 460(i)), Crospovidone (INS 1202), Hydroxypropyl Cellulose (INS 463), Croscarmellose Sodium (INS 466), Hydroxypropyl methyl cellulose (INS 464), Talc (INS 553(iii)), Vitamin D_3, Colloidal Silicon Dioxide (INS 551), Magnesium Stearate, Polyethylene glycol (INS 1521), Pyridoxal-5-Phosphate, Sodium Methyl Paraben, Ethyl

Cellulose (INS 462), Folic Acid, Butylated Hydroxy Anisole (INS 320), Butylated Hydroxy Toluene (INS 321), Cyanocobalamin and Propyl Paraben Sodium.

Contains Permitted Natural Colours (Titanium Dioxide (INS 171), Red Iron Oxide (NS 172(ii)) and Added Artificial Flavouring Substance (Vanilla Flavour).

8. Pharmaceutical particulars:

8.1 Incompatibilities:

Not applicable.

8.2 Shelf-life:

Best before 18 months from manufacture.

8.3 Packaging information:

SHELCAL MOM is packed in blister strip of 15 tablets.

8.4 Storage and handing instructions:

Store below 30°C.

Keep out of reach of children.

9. Patient Counselling Information

Package leaflet: Information for the user
SHELCAL MOM
Calcium Carbonate, Pyridoxal-5-Phosphate, Folic Acid, Vitamin D3, Cyanocobalamin with Docosahexaenoic Acid (DHA) Tablets

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet?

9.1. What is and what it is used for

The main ingredient is Calcium Carbonate, Pyridoxal-5-Phosphate, Folic Acid, Vitamin D_3, Cyanocobalamin with Docosahexaenoic Acid (DHA) Tablets.

Shelcal MOM is indicated in the management of associated deficiencies of Calcium, Folic Acid, Cyanocobalamin and vitamin D_3 in pregnancy.

9.2. What you need to know before you use SHELCAL MOM

Do not take SHELCAL MOM :

- If you are hypersensitive to the active substances or to any of the excipients.
- If you have diseases and/or conditions resulting in in hypercalcaemia and/or hypercalciuria (e.g. myeloma, bone metastases, primary hyperparathyroidism).
- If you have Nephrolithiasis
- If you have Renal failure
- If you have Hypervitaminosis D
- If you have Sarcoidosis
- If you have primary hyperparathyroidism and vitamin D over dosage.
- If you have osteoporosis due to prolonged immobilisation, renal stones.

Warnings and precautions

Talk to your doctor or pharmacist before taking SHELCAL MOM. Inform your doctor if you have or develop any problem :

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 or diuretics 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 D_3 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 D_3 in the form of Cholecalciferol is not metabolised normally and other forms of Vitamin D_3 should be used. Should be prescribed with caution to patients suffering from sarcoidosis because of the risk of increased metabolism of Vitamin D_3 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 D_3 or nutrients (such as milk). Additional doses of calcium or Vitamin D_3 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.

Patients with vitamin B_{12} deficiency should not be treated with folic acid unless administered with adequate amounts of hydroxocobalamin, as it can mask the condition but the subacute irreversible damage to the nervous system will continue. The deficiency can be due to undiagnosed megaloblastic anaemia including in infancy, pernicious anaemia or macrocytic anaemia of unknown aethiology or other cause of cobalamin deficiency, including lifelong vegetarians. Therefore, a full clinical diagnosis should be made before initiating treatment. Folate should not be routinely used in patients receiving coronary stents. Caution should be exercised when administering folic acid to patients who may have folate dependent tumours. Folic acid is removed by haemodialysis. Patients with rare hereditary problems of galactose intolerance, the lapp lactase deficiency or glucose – galactose malabsorption should not take this medicine.

Patients with early Leber's disease (hereditary optic nerve atrophy) who were treated with vitamin B_{12} suffered severe and swift optic atrophy. Hypokalemia and sudden death may occur in severe megaloblastic anemia which is treated intensely with vitamin B_{12}. Folic acid is not a substitute for vitamin B_{12} although it may improve vitamin B_{12}-deficient megaloblastic anemia. Exclusive use of folic acid in treating vitamin B_{12}- deficient megaloblastic anemia could result in progressive and irreversible neurologic damage. Blunted or impeded therapeutic response to

vitamin B_{12} may be due to such conditions as infection, uremia and drugs having bone marrow suppressant properties such as chloramphenicol, and concurrent iron or folic acid deficiency. Doses of vitamin B_{12} exceeding 10 mcg daily may produce hematologic response in patients with folate deficiency. Indiscriminate administration may mask the true diagnosis. The validity of diagnostic vitamin B_{12} or folic acid blood assays could be compromised by medications, and this should be considered before relying on such tests for therapy. Vitamin B_{12} is not a substitute for folic acid and since it might improve folic acid deficient megaloblastic anemia, indiscriminate use of vitamin B_{12} could mask the true diagnosis.

Hypokalemia and thrombocytosis could occur upon conversion of severe megaloblastic to normal erythropoiesis with vitamin B_{12} therapy. Therefore, serum potassium levels and the platelet count should be monitored carefully during therapy. Vitamin B_{12} deficiency may suppress the signs of polycythemia vera. Treatment with vitamin B_{12} may unmask this condition.

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. Certain medicines cannot be used at the same time, while other drugs require specific changes (in the dose, for example).

Always tell your doctor if you are using or receiving any of the following medicines in addition to SHELCAL MOM:

- 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.
- SHELCAL MOM 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 D_3.
- 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.
- Caution should be exercised when administering SHELCAL MOM to epileptics. It may cause reduction in the plasma concentrations of phenytoin, primidone, phenobarbital, sodium valproate, carbamazepine and the barbiturates. Trimethoprim or sulfonamides, alone or in combination as co-trimoxazole, may reduce the effect of folic acid and this may be serious in patients with megaloblastic anaemia. Sulphasalazine and triamterene can reduce the absorption of folic acid. Folic acid may interfere with the toxic and therapeutic effects of methotrexate. Methotrexate and trimethoprim are specific anti-folates and the folate

deficiency caused by their prolonged use cannot be treated by Folic Acid Tablets. Folinic acid should be used. Folate supplements enhance the efficacy of lithium therapy. Nitrous oxide anaesthesia may cause an acute folic acid deficiency. Both ethanol and aspirin increase folic elimination. Concurrent administration with cholestyramine may interfere with folic acid absorption. Patients on prolonged cholestyramine therapy should take folic acid 1 hour before or 4 to 6 hours after receiving cholestyramine. Antibiotics may interfere with the microbiological assay for serum and erythrocyte folic acid concentrations and may cause falsely low results. Fluorouracil toxicity may occur in patients taking folic acid and this combination should be avoided. Edible clay or antacids containing aluminium or magnesium may reduce folic acid absorption. Patients should be advised to take antacids at least two hours after administration of folic acid. Folic acid may reduce intestinal absorption of zinc (of particular importance in pregnancy).

- Absorption may be reduced by Para-aminosalicylic acid, colchinine, biguanides, neomycin, cholestyramine, potassium chloride, methyldopa, and cimetidine. Patients treated with chloramphenicol may respond poorly to this medicine. Serum levels of this medicine may be lowered by oral contraceptives. These interactions are unlikely to have clinical significance. Anti-metabolities and most antibiotics invalidate vitamins B_{12} assays by microbiological techniques.
- SHELCAL MOM 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 a preparation containing both carbidopa and levodopa.

Pregnancy, breast-feeding and fertility

In pregnant women, overdoses of Shelcal MOM should be avoided as permanent hypercalcaemia has been related to adverse effects on the developing foetus. Shelcal MOM tablets can be used during breast-feeding. Shelcal MOM pass into breast milk. This should be considered when giving additional Vitamin D3 to the child.

Interference with folic acid metabolism or folate deficiency induced by drugs such as anticonvulsants and some antineoplastics early in pregnancy results in congenital anomalies. Lack of the vitamin or its metabolites may also be responsible for some cases of spontaneous abortion and intrauterine growth retardation.

Imbalance in folate requiring trophoblast cells may also lead to detachment of the placenta.

Driving and using machines

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

9.3. How to use SHELCAL MOM

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. SHELCAL MOM is best taken with some water.

Use in children and adolescents
SHELCAL MOM is not recommended in children and adolescents.

If you take more SHELCAL MOM than you should

If you take more SHELCAL MOM than prescribed by your doctor, talk to your doctor or pharmacist straight away. The most frequent symptoms and signs of a SHELCAL MOM overdose is hypervitaminosis D, hypercalcaemia, 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.

If you forget to take SHELCAL MOM
If you forget to take your medicine, but remember a little later on that you should have taken it; take that day's dose as usual. However, if a long delay has occurred (e.g. several hours), so that the next due dose is near, skip the forgotten dose and take the next dose the next, scheduled, normal dose at the usual time. Do not take a double dose to make up for a forgotten dose. Repeated skipping, however, should be avoided.

9.4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. When SHELCAL MOM tablets are used as supplement, the possible side effects are:

Hypercalcaemia and hypercalciuria, Constipation, dyspepsia, flatulence, nausea, abdominal pain and diarrhoea. Skin and subcutaneous disorders Rare: Pruritus, rash and urticarial, anemia, cough, CNS depression, drowsiness, headache, heart damage, lassitude (weakness, exhaustion), liver damage, narcosis, reproductive effects and teratogenic effects, Anorexia, nausea, abdominal distension and flatulence, Allergic reactions, comprising erythema, rash, pruritus, urticaria, dyspnoea, and anaphylactic reactions (including shock), itching exanthema, and exceptionally as anaphylactic shock, Acne form and bullous eruptions, Paresthesia, somnolence, and headaches have been reported.

Reporting of side effects:

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:
http://www.torrentpharma.com/index.php/site/info/adverse_event_reporting

9.5. How to store SHELCAL MOM

Store below 30°C.
Keep out of reach of children.

9.6. Contents of the pack and other information

What SHELCAL MOM contains

The main ingredients are Calcium Carbonate, Pyridoxal 5'-Phosphate, Folic Acid, Vitamin D_3, Cyanocobalamin with Docosahexaenoic Acid (DHA) Tablets.
The ingredients are Calcium Carbonate, Docosahexaenoic Acid, Microcrystalline Cellulose (INS 460(i)), Crospovidone (INS 1202), Hydroxypropyl Cellulose (INS 463), Croscarmellose Sodium (INS 466), Hydroxypropyl methyl cellulose (INS 464), Talc (INS 553(iii)), Vitamin D_3, Colloidal Silicon Dioxide (INS 551), Magnesium Stearate, Polyethylene glycol (INS 1521), Pyridoxal-5-Phosphate, Sodium Methyl Paraben, Ethyl Cellulose (INS 462), Folic Acid, Butylated Hydroxy Anisole (INS 320), Butylated Hydroxy Toluene (INS 321), Cyanocobalamin and Propyl Paraben Sodium.
Contains Permitted Natural Colours (Titanium Dioxide (INS 171), Red Iron Oxide (NS 172(ii)) and Added Artificial Flavouring Substance (Vanilla Flavour).

Nutritional Information* per 100g (Approx.):		
Energy	120.736	Kcal
Fat	1.139	g
Protein	2.061	g
Carbohydrate	25.559	g
(Sugar)	30.310	g

*Approximate values when packed.

NUTRACEUTICAL

- This product is not intended to diagnose, treat, cure or prevent any disease. In case you are pregnant, lactating or taking any medication, consult your Healthcare Professional.
- Not to exceed the stated recommended daily usage.
- Not recommended for children.
- Recommended Usage: One tablet a day or as directed by the Healthcare Professional.
- NOT FOR MEDICINAL USE
- Keep out of reach of children.

10. Details of manufacturer

Manufactured by:
Ravenbhel Healthcare Pvt Ltd.
16-17, EPIP, SIDCO, Kartholi, Bari-Brahmana, Jammu – 181133.
OR
Manufactured by:
Maxcure Nutravedics Ltd.
Plot No-13, Sector-6A, I.I.E, SIDCUL, Ranipur, Haridwar, Uttarakhand-249403.

11. Details of permission or licence number with date

Ravenbhel Healthcare Pvt Ltd

FSSAI Lic No. 10014061000240 issued on 20.04.2020

Maxcure Nutravedics Ltd.

FSSAI Lic No. 10016012000340 issued on 20.01.2021

12. Date of revision

NA

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TORRENT PHARMACEUTICALS LTD.

IN/ SHELCAL MOM 500 mg, 2.5 mg, 294 mcg, 400 IU, 1.2 mcg, 150 mg /JAN-21/01/PI