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

CCM TABLETS

1. GENERIC NAME

Calcium Citrate Malate, Vitamin D_3 and Folic Acid Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains:

Calcium Citrate Malate IP equivalent to Calcium 250 mg
Cholecalciferol Concentrate (Powder Form) IP equivalent to Cholecalciferol (Vitamin D_3) 100 IU
Folic Acid IP 50 mcg
Excipients q.s.
Colour: Titanium Dioxide IP
Appropriate overages added for vitamins

List of Excipients

Maize Starch, Polyvinylpyrrolidone K-30, Colloidal Silicon Dioxide and Magnesium Stearate, Methyl Hydroxybenzoate (Methyl Paraben) and Propyl Hydroxybenzoate (Propyl Paraben), Purified water* (*evaporates during processing).

Film-Coating:
Instacoat Universal (contains: Hydroxy propyl methyl cellulose, Polyethylene glycol, Talc, colourant - Titanium dioxide).

3. DOSAGE FORM AND STRENGTH

Film-coated tablets.
For information on strength refer *section 2. Qualitative and Quantitative Composition* above.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

For the treatment of calcium and vitamin D deficiency states (pregnancy, lactation, growing children).

4.2 Posology and Method of Administration

For oral use.

The duration of therapy depends on the response to therapy.

Adults

2 tablets twice daily.

Children

2 tablets per day in one or two divided doses.

The ability of the child to take *CCM TABLETS* should be taken into account before prescribing it to children, particularly to young children.

Renal impairment

CCM TABLETS should be used with caution in patients with renal impairment (*see section 4.4 Special Warnings and Precautions for Use*). Use in patients with renal failure is contraindicated (*see 4.3 Contraindications*).

Hepatic Impairment

No dose adjustment is required.

4.3 Contraindications

CCM TABLETS are contraindicated in:

- Hypersensitivity to the active substances or to any of the excipients listed in *section 2*.
- Hypercalciuria, hypercalcaemia and disease and/or conditions which lead to hypercalcaemia and/or hypercalciuria (e.g. primary hyperparathyroidism, myeloma, bone metastases).
- Nephrolithiasis.
- Nephrocalcinosis
- Hypervitaminosis D.
- Renal failure .

4.4 Special Warnings and Precautions for Use

Monitoring of Calcium Levels

During long-term treatment, serum calcium levels should be followed and renal function should be monitored through measurements of serum creatinine. Monitoring is especially important in patients on concomitant treatment with cardiac glycosides or thiazide diuretics (*see 4.5 Drug Interactions*) and in patients with a high tendency to calculus formation.
If signs of hypercalcaemia and/or hypercalciuria occur treatment must be discontinued. Treatment should be reduced or temporarily stopped, if urinary calcium level exceeds 7.5 mmol/24 h (300 mg/24 h) in adults.

Sarcoidosis

CCM TABLETS should be prescribed with caution to patients suffering from sarcoidosis, due to the risk of increased metabolism of vitamin D into its active form. These patients should be monitored with regard to the calcium content in serum and urine.

Immobilised patients with Osteoporosis

CCM TABLETS should be used cautiously in immobilised patients with osteoporosis due to increased risk of hypercalcaemia.

Renal impairment

CCM TABLETS should be used with caution in patients with renal impairment and the effect on calcium and phosphate levels should be monitored. Patients with renal impairment are at potential risk of hyperphosphaetemia, nephrolithiasis and nephrocalcinosis. The risk of soft tissue calcification should be taken into account. In patients with severe renal impairment, vitamin D in the form of cholecalciferol

might not be activated normally. The physician may decide if other forms of vitamin D should be supplemented (*see 4.2Posology and Method of Administration).*

Milk-alkali syndrome

Milk-alkali syndrome (Burnett´s syndrome) i.e. hypercalcemia, alkalosis and renal impairment, can develop when large amounts of calcium are ingested with absorbable alkali.

Other medicinal products containing calcium or vitamin D

The content of vitamin D in *CCM TABLETS* should be considered when prescribing other medicinal products containing vitamin D. Additional doses of calcium or vitamin D should be taken under close medical supervision. In such cases it is necessary to monitor serum calcium levels and urinary calcium excretion frequently. Calcium and vitamin D intake from other sources (food, dietary supplements) should be estimated, before prescribing the product.

Tetracyclines or quinolones

Co-administration with tetracyclines or quinolones is usually not recommended, or must be done with precaution (*see 4.5 Drug Interactions*).

4.5 Drug Interactions

Phenytoin, barbiturates

Concomitant use of phenytoin or barbiturates may reduce the effect of vitamin D_3 since the metabolism increases.

Antiepileptics

Folic acid has been reported to decrease serum concentrations of phenobarbital and phenytoin. Antiepileptics may produce folate deficiency states. Replacement therapy with folinic acid or folic acid may become necessary during antiepileptic therapy in order to prevent development of megaloblastic anaemia

Thiazide diuretics

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.

Corticosteroids

Systemic corticosteroids reduce calcium absorption. During concomitant use, it may be necessary to increase the dose of *CCM TABLETS.*

Ion exchange resins, liquid paraffin

Simultaneous treatment with ion exchange resins such as cholestyramine or laxatives such as paraffin oil may reduce the gastrointestinal absorption of vitamin D. Therefore a time interval as long as possible between the intakes should be recommended.

Tetracyclines

Calcium 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.

Quinolone

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

Penicillamine & Isoniazid

Penicillamine (a chelating agent) and antituberculous drugs (such as isoniazid) may increase the requirements for folic acid.

Cardiac glycosides

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

Bisphosphonate

If a bisphosphonate is used concomitantly, this preparation should be administered at least one hour before the intake of *CCM TABLETS* since gastrointestinal absorption of may be reduced.

Sodium fluoride

Calcium may also reduce absorption of sodium fluoride and such preparations should be administered at least three hours before the intake of *CCM TABLETS*.

Iron, zinc and strontium ranelate

Calcium salts may decrease the absorption of iron, zinc and strontium ranelate. Consequently, iron, zinc or strontium ranelate preparations should be taken at least two hours before or after calcium/cholecalciferol.

Oxalic acid, phytic acid

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

Levothyroxine

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.

Estramustine

Calcium reduces the gastrointestinal absorption of estramustine by formation of an insoluble complex. Consequently, administration of *CCM TABLETS* and estramustine containing products should be separated by at least two hours.

Glucarpidase

Folate deficiency states may be produced by glucarpidase.

Folic acid antagonists

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

Oral contraceptives

Serum concentration of folic acid may be decreased by use of oral contraceptives.

Alcohol

Alcohol may produce folate deficiency states.

Orlistat

Treatment with orlistat may potentially impair the absorption of fat-soluble vitamins, e.g. vitamin D_3.

4.6 Use in Special Populations

Fertility

Normal endogenous levels of calcium and vitamin D are not expected to have any adverse effects on fertility.

Pregnancy

Studies in animals have shown reproductive toxicity of high doses of vitamin D.

In pregnant women, overdoses of calcium and vitamin D should be avoided, as permanent hypercalcaemia has been related to adverse effects on developing foetus.

Lactation

Calcium /cholecalciferol can be used during breast-feeding.

Calcium passes slightly into breast-milk, without having a negative effect on children.

Vitamin D and its metabolites also pass into breast-milk. This should be considered when giving additional vitamin D to the child.

4.7 Effects on Ability to Drive and Use Machines

An unfavourable effect of *CCM TABLETS* on the ability to drive or operate machines is very unlikely.

4.8 Undesirable Effects

Clinical Trial Data

There are no relevant data available

Post Marketing Data

Adverse drug reactions (ADRs) are listed below by MedDRA system organ class and by frequency.

Frequencies are defined as:

Very common ≥1/10
Common ≥1/100 to <1/10
Uncommon ≥1/1000 to <1/100
Rare ≥1/10000 to <1/1000
Very rare <1/10000
Not known (cannot be estimated from the available data).

Immune system disorders
Not known: hypersensitivity reactions *(see Skin and subcutaneous tissue disorders; Respiratory, thoracic and mediastinal disorders),* anaphylactic reaction.

Metabolism and nutrition disorders
Uncommon: hypercalcaemia, hypercalciuria.
Very rare: Milk-alkali syndrome, see usually only in overdose.

Respiratory, thoracic and mediastinal disorders
Not known: laryngeal oedema.

Gastrointestinal disorders
Rare: nausea, diarrhea, abdominal pain, constipation, flatulence, abdominal distension.
Not known: vomiting.

Skin and subcutaneous tissue disorders
Rare: rash, pruritus, urticaria.
Not known: angioedema.

4.9 Overdose

Symptoms and signs

Overdosage can lead to hypervitaminosis and hypercalcaemia. Symptoms of hypercalcaemia may include anorexia, nausea, vomiting, thirst, polydipsia, polyuria, constipation, abdominal pain, muscle weakness, fatigue, mental disturbances, bone pain, nephrocalcinosis, renal calculi and in severe cases cardiac arrythmias. Extreme hypercalcemia may result in coma and death. Persistently high calcium levels may lead to irreversible renal damage and soft tissue calcification.

Milk-alkali syndrome may occur in patients who ingest large amounts of calcium and absorbable alkali. Symptoms are frequent urge to urinate, continuing headache, continuing loss of appetite, nausea or vomiting, unusual tiredness or weakness, hypercalcaemia, alkalosis and renal impairment.

The threshold for vitamin D intoxication is between 40,000 and 100,000 I.U./day for 1-2 months in persons with normal parathyroid function, for calcium in excess of 2000 mg per day.

Treatment

In the case of intoxication, treatment should be stopped immediately and the fluid deficiency should be balanced. Treatment with thiazide diuretics, lithium, vitamin A, vitamin D and cardiac glycosides must also be discontinued.

Rehydration and, according to severity, isolated or combined treatment with loop diuretics, bisphosphonates, calcitonin and corticosteroids should be given. Serum electrolytes, renal function and diuresis must be monitored. In severe cases ECG and CVP should be followed.

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

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action and Pharmacodynamic Properties

Calcium
Calcium is the fifth most abundant element in the body and is a major substrate for mineralization and antiresorptive effect on bone. Calcium is a divalent metal essential for the maintenance of the nervous, muscular, and skeletal systems, as well as for cell membrane and capillary permeability. Its role in bone structure and muscle contraction is well known, but calcium is also important for blood coagulation, nerve conduction, and electrical conduction in the heart. More than 99% of total body calcium is stored in bones and teeth where it functions to support their structure. Parathyroid hormone (PTH), vitamin D, and, to a lesser extent, calcitonin, glucocorticoids, and magnesium, influence calcium balance. Calcium suppresses PTH secretion, decreasing bone turnover. Increased levels of PTH have been found to be a contributory factor to age related bone loss, especially at cortical sites. Increased bone turnover is an independent risk factor for fractures. When calcium intake is low or calcium absorption is disrupted, bone resorption occurs at a faster rate than bone formation, because the body must use the calcium stored in bones to maintain normal biological processes such as nerve and muscle function. Osteoporosis and osteopenia can result from several factors including chronically low calcium intake, low vitamin D intake, poor calcium absorption, and/or excess calcium excretion.

Vitamin D
Activated vitamin D promotes renal reabsorption of calcium, increases intestinal absorption of calcium and phosphorus, and increases calcium and phosphorus mobilization from bone to plasma. Vitamin D is biologically inert and requires hydroxylation in the body to form the active metabolite. The activated form of vitamin D acts similarly to calcitriol, an active vitamin D analog, in that it appears to promote intestinal absorption of calcium through binding to a specific receptor in the mucosal cytoplasm of the intestine. Subsequently, calcium is absorbed through formation of a calcium-binding protein. Additionally, vitamin D has been studied as an independent factor in promoting skeletal strength by increasing muscle fiber growth and in balance by reducing body sway; a meta-analysis found supplementation with vitamin D reduced the risk of falls in an elderly population by 20 percent. Some evidence suggests that the active moiety of vitamin D acts at the level of the cell nucleus to increase plasma calcium and phosphorus. Once plasma saturation of these electrolytes occurs, bone mineralization takes place. The synthesis of activated vitamin D is enhanced by elevated parathyroid hormone levels and low plasma phosphorus levels. Hypocalcemia causes release of parathyroid hormone, which stimulates the production of activated vitamin D.

Folic acid
Folic acid, a biochemically inactive compound, is the precursor for tetrahydrofolic acid and methyltetrahydrofolate. Tetrahydrofolic acid, methyltetrahydrofolate, and other folic acid congeners are essential for the maintenance of normal erythropoiesis and are also required cofactors for the synthesis of purine and thymidylate nucleic acids. They are also necessary for the interconversion of amino acids such as the metabolism of histidine to glutamic acid and the interconversion of serine and glycine. Folic

acid congeners are transported across cells by receptor-mediated endocytosis where they function and are stored. Other processes involving folate coenzymes include generation and use of formate and methylation of transfer RNA. Impaired thymidylate synthesis, which leads to faulty DNA synthesis, is responsible for megaloblastic and macrocytic anemias.

An important role of folic acid is the formation of methionine from homocysteine using vitamin B12 as a cofactor. Adequate folic acid intakes can normalize high homocysteine levels via increased remethylation of homocysteine to methionine via 5-methyltetrahydrofolate-homocysteine methyltransferase (a.k.a.; methionine synthetase). Reduced folic acid intake is associated with hyperhomocysteinemia. Hyperhomocysteinemia is recognized as an independent risk factor for artherosclerosis of the coronary, cerebral, and peripheral vasculature. There is mounting evidence that elevated plasma homocysteine (and therefore decreased serum methionine) contributes to congenital neural tube defects. High serum homocysteine levels may also be important in the pathogenesis of colon cancer, diabetic retinopathy, and other diseases.

5.2 Pharmacokinetic Properties

Calcium
In general, the absorption of calcium from the intestine is never complete and demands that the calcium be in a soluble, ionized form. Oral bioavailability is influenced by the intestinal pH, the presence of food, the dosage administered, and the presence of calcium deficiency; absorption is increased in patients with calcium deficiency or low-calcium diets. Bioavailability is also influenced by the hormonal influence of PTH and vitamin D. The normal bioavailability of calcium from supplements is usually only 25—35%. The intestinal pH for dissolution and absorption of calcium salts and complexes is typically in the optimal range of 5—7, shortly after a meal in the patient with normal stomach acid status. Thus, it is often recommended that calcium be administered with or up to 1.5 hours after a meal to enhance absorption of the supplement. In patients with achlorhydria or other conditions of low stomach acid, calcium absorption is enhanced by taking the supplement with meals versus after meals so that the small amount of acid produced to aid digestion can also help aid calcium absorption. The anions (i.e., oxalate, phylates, or sulfates) or high fiber percentage present in certain foods may reduce the bioavailability of calcium.
Calcium is excreted in the urine (roughly 20%); urinary excretion of calcium is often measured as a marker for calcium bioavailability in clinical studies. The amount excreted in the urine varies with the degree of calcium absorption, the rate of bone turnover, and renal conservation status. The fecal excretion of calcium is roughly 80% and represents primarily nonabsorbed calcium remaining in the gut.

Vitamin D
Oral absorption of vitamin D occurs rapidly and completely in the presence of bile salts. The onset of action following oral administration is 10—24 hours, with maximal effects usually observed in 4 weeks. Vitamin D enters the blood through chylomicrons of lymph. Vitamin D is stored primarily in the liver and fat depots. The parent compound and its metabolites are bound in plasma to alpha-globulins. Vitamin D is converted in the liver by the enzyme vitamin D-25-hydroxylase (cytochrome P450 27) to 25-hydroxyergocalciferol, an active, intermediate. Vitamin D is further converted to its most active form, 1,25-dihydroxyergocalciferol, in the kidneys. The intermediate metabolite of Vitamin D may be distributed into breast milk following high doses. All of the metabolites of vitamin D have not been identified. Elimination of vitamin D and its metabolites occurs principally through the bile, with the remainder excreted renally. The half-life is 19—48 hours.

Folic acid
Following oral administration, folic acid is rapidly absorbed from the small intestine. Because dietary folate is primarily in the polyglutamyl form, it must be converted to the monoglutamate form by intestinal conjugase enzymes prior to absorption. The monoglutamate form is then reduced and methylated to methyltetrahydrofolate by dihydrofolate reductase during transport across the intestinal mucosa. Absorption of dietary folic acid is impaired in the presence of malabsorption syndromes;

however, the absorption of synthetic, commercially available folic acid is unaffected. The peak activity of this vitamin occurs within 1 hour.
Folic acid congeners are extensively bound to plasma proteins and are distributed throughout the body including the CSF. They also appear in breast milk. After administration of small doses, reduction and methylation of folic acid to methyltetrahydrofolate occurs in the liver. Following large doses, folic acid may appear unchanged in the plasma. Active forms of folic acid are reabsorbed through enterohepatic recirculation. Folic acid is eliminated primarily renally as metabolites. When body stores become saturated, excess folic acid is excreted unchanged in the urine.

6. NONCLINICAL PROPERTIES

At vitamin D doses far higher than the human therapeutic range teratogenicity has been observed in animal studies.

7. DESCRIPTION

Film-coated tablets.

Calcium Citrate Malate IP equivalent to
Calcium 250 mg
Cholecalciferol Concentrate (Powder Form) IP equivalent to Cholecalciferol (Vitamin D_3) 100 IU
Folic Acid IP 50 mcg
Excipients q.s.
Colour: Titanium Dioxide IP
Appropriate overages added for vitamins

List of Excipients

Maize Starch, Polyvinylpyrrolidone K-30, Colloidal Silicon Dioxide and Magnesium Stearate, Methyl Hydroxybenzoate (Methyl Paraben) and propyl hydroxybenzoate (Propyl Paraben), Purified water* (*evaporates during processing).

Film-Coating:
Instacoat Universal (contains: Hydroxy propyl methyl cellulose, Polyethylene glycol, Talc, colourant - Titanium dioxide).

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

There are no relevant data available.

8.2 Shelf Life

The expiry date is indicated on the label and packaging.

8.3 Packaging Information

Tablets packed in a HDPE bottle.

8.4 Storage and Handling Instructions

Store the container well closed at temperature not exceeding 30°C. Protect from light and moisture.
Keep out of reach of children.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or their patients' caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contraindications of *CCM TABLETS*. Patients (and/or their patients' caregiver) may also be informed about posology, method of administration and storage/handling information as applicable.

10. DETAILS OF MANUFACTURER

The Manufacturing Site details are mentioned on the label and packaging.

For further information please contact:
GlaxoSmithKline Pharmaceuticals Limited,
Registered Office
Dr. Annie Besant Road, Worli
Mumbai 400 030, India.

11. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE

Manufacturing License number is indicated on the label and packaging.

12. DATE OF REVISION

01-JUL-2026

Version: CCM/PI/IN/2026/01

Adapted from:

- *Kalcipos-D 500 mg/ 800 IU chewable tablets SmPC (date of revision: 15/07/2025). Available from: https://mhraproducts4853.blob.core.windows.net/docs/71baa5a8e2d5c3647f888ec2b49140a7d7ca187b*
- *Calcium + Cholecalciferol NCDS Version number 05 dated 21 October 2019 (obsolete)*
- *Theragran Stress NCDS Version number 04 dated 16 December 2019*
- *Clinical Pharmacology – Calcium citrate malate 500 mg with D_3 tablet monograph. Available from: https://www.clinicalkey.com/pharmacology/monograph/3466?aprid=81864*
- *Clinical Pharmacology – Folic acid, Vit B9 monograph. Available from: https://www.clinicalkey.com/pharmacology/monograph/266*