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

BECADEXAMIN

1. GENERIC NAME

Multivitamin and Multimineral Capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Soft Gelatin capsule contains:

Vitamin A (as Vitamin A Concentrate Oil IP)	5000 IU
Vitamin D_3 (Cholecalciferol IP)	400 IU
Vitamin E (Tocopheryl Acetate IP)	15 mg
Vitamin B_1 IP	5 mg
Vitamin B_2 IP	5 mg
Nicotinamide IP	45 mg
D-Panthenol IP	5 mg
Vitamin B_6 IP	2 mg
Vitamin C IP	75 mg
Folic Acid IP	1000 mcg
Vitamin B_{12} IP	5 mcg
Dibasic Calcium Phosphate IP	70 mg
Copper Sulfate Pentahydrate BP	0.1 mg
Manganese Sulfate Monohydrate BP	0.01 mg
Zinc Sulphate Monohydrate IP	28.7 mg (equivalent to 10.4 mg of elemental Zinc)
Potassium Iodide IP	0.025 mg
Light Magnesium Oxide IP	0.15 mg

(Appropriate overages added)
Excipients q.s.
Approved colours used in empty gelatin capsule shell

List of Excipients
Lecithin Soyabean, Partially Hydrogenated Vegetable Oil, Yellow Beeswax, Arachis oil. Gelatin mass for soft gelatin capsule contains Gelatin, Glycerin, Purified water, Ethyl Vanillin, Methyl Hydroxybenzoate, Ethyl Hydroxybenzoate, Propyl Hydroxybenzoate. Capsule shell contains colours Sunset Yellow FCF, Brilliant Blue FCF, Erythrosine, Ponceau 4R and Titanium Dioxide.

3. DOSAGE FORM AND STRENGTH

Soft Gelatin capsules for oral administration.
For information on strength refer *2. Qualitative and Quantitative Composition* above.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

BECADEXAMIN is indicated for the treatment of vitamins and minerals deficiency states in adults which may be associated with the following conditions:

- Unbalanced diet
- Infections
- Convalescence
- Old age

4.2 Posology and Method of Administration

Adults

For oral administration. One capsule once daily.

Duration of treatment depends on the improvement of the deficiency states.

Children

BECADEXAMIN is not recommended for paediatric use.

Elderly

There are no relevant data available.

Renal Impairment

Caution should be exercised when using *BECADEXAMIN* in patients with renal disorders (see *4.4 Special Warnings and Precautions for Use*).

Hepatic Impairment

Caution should be exercised when using *BECADEXAMIN* in patients with hepatic disorders (see *4.4 Special Warnings and Precautions for Use*).

4.3 Contraindications

BECADEXAMIN is contraindicated in:

- Hypersensitivity to any of the components,
- Treatment with retinoids (see 4.5 *Drug Interaction*)

4.4 Special Warnings and Precautions for Use

Concomitant conditions

Caution should be used in case of the following concomitant conditions:

- hepatitis or hepatic disorders,

- kidney disorders,
- intestinal stricture inflammation,
- active duodenal or gastric ulcer,
- diabetes mellitus.

High dose of nicotinamide should be used with caution in patients with peptic ulcer disease, gastritis, liver disease, gall bladder disease, diabetes and gout.

Gastrointestinal symptoms
Patients with ostomies may have altered intestinal transit times.

Cardiac disorders
BECADEXAMIN should be used with caution in the presence of cardiac disease, as it contains vitamin D.

Vision disorders
Cyanocobalamin (vitamin B_{12}) should not be used for Leber's disease or tobacco amblyopia since these optic neuropathies may degenerate further.

Hypercalcaemia
BECADEXAMIN is not recommended for patients with hypercalcaemia or diseases associated with hypercalcaemia such as sarcoidosis and some malignancies, as it contains calcium and vitamin D. It should be given cautiously to these patients.

Effects on the thyroid
Although iodine is required for the production of thyroid hormones, excessive quantities can cause hyperthyroidism, or even paradoxical goitre and hypothyroidism (see 4.8 *Undesirable Effects).*

Investigations
As iodine and iodides can affect the thyroid gland, their use may interfere with tests of thyroid function.

Large doses of riboflavin (vitamin B_2) result in a bright yellow discoloration of the urine that may interfere with certain laboratory tests.

Ascorbic acid, a strong reducing agent, interferes with laboratory tests involving oxidation and reduction reactions. Falsely-elevated or false-negative test results may be obtained from plasma, faeces, or urine samples depending on such factors as the dose of ascorbic acid and specific method used.

Long-term treatment
Caution is necessary if preparations containing iodine or iodides are taken for long periods.

Long-term use of large doses of pyridoxine (vitamin B_6) is associated with the development of severe peripheral neuropathies; the dose at which these occur is not established.

The use of excessive amounts of vitamin A substances over long periods can lead to toxicity (see 4.9 *Overdose).*

Risk of overdosage
Other medicinal product containing vitamin A should not be used while taking *BECADEXAMIN* as it may cause overdose symptoms (see 4.5 *Drug Interaction;* 4.9 *Overdose*).

Overdose symptoms may occur as a result of prolonged (several weeks or months) administration of doses starting from 10,000 IU daily, in patients with liver or kidney impairment, low body weight, hypoproteinemia and alcohol abuse *(*see 4.9 *Overdose)*.

Other medicinal product containing vitamin E should not be used while taking this product as it may cause overdose symptoms *(*see 4.9 *Overdose).*

Treatment preparation and monitoring
BECADEXAMIN should, if possible, not be given to patients with suspected vitamin B_{12} deficiency without first confirming the diagnosis.

Plasma phosphate concentrations should be controlled during vitamin D therapy to reduce the risk of ectopic calcification.

Tolerance
Tolerance may be induced with prolonged use of large doses of vitamin C, resulting in symptoms of deficiency when intake is reduced to normal.

4.5 Drug Interaction

Diuretics
As *BECADEXAMIN* contains calcium and vitamin D, hypercalcaemia may occur when it is given with thiazide diuretics.

Thiazide diuretics decrease urinary excretion of calcium. Plasma-calcium concentrations should be monitored in patients receiving the drugs together.

Corticosteroids
Corticosteroids reduce calcium absorption.
Corticosteroids may counteract the effect of vitamin D.

Cardiac glycosides
Calcium enhances the effects of digitalis glycosides on the heart and may precipitate digitalis intoxication.

Antibiotics
Zinc supplements also reduce the absorption of fluoroquinolones.

Tetracycline antibiotics, other than doxycycline also decrease zinc absorption, they should therefore be administered 2 hours before or 3 hours after the administration of *BECADEXAMIN*, in those cases where concomitant use is necessary.

Calcium salts reduce the absorption of some fluoroquinolones, and tetracyclines therefore, doses should be separated by at least 3 hours.

Penicillamine (a chelating agent) may reduce the absorption of zinc.

Penicillamine and antituberculous drugs (such as isoniazid) may increase the requirements for folic acid and pyridoxine (vitamin B_6).

Neomycin used orally may reduce the absorption of vitamin A, vitamin B_{12} and vitamin E.

Rifampicin and isoniazid may reduce the effectiveness of vitamin D.

Bisphosphonates
As *BECADEXAMIN* contains calcium and magnesium salts, it reduces the absorption of bisphosphonates, therefore doses should be separated by at least 3 hours.

Folic acid antagonists
Folate deficiency states may be produced by drugs such as antiepileptics, oral contraceptives, antituberculous drugs, alcohol, glucarpidase, and folic acid antagonists such as methotrexate, pyrimethamine, triamterene, trimethoprim and sulfonamides.

Amiodarone
The effects of iodine and iodides on the thyroid may be altered by other compounds including amiodarone.

Cholestyramine, colestipol and mineral oils and orlistat
Cholestyramine, colestipol and mineral oils used orally may reduce the absorption of vitamin A and vitamin E.

Orlistat may interfere with the absorption of vitamin E.

Retinoids
Combined treatment with retinoids (isotretinoin, etretinate, bexarotene) and vitamin A in doses exceeding 4000–5000 IU daily may induce vitamin A overdose symptoms (see 4.4 *Special Warnings and Precautions for Use;* 4.9 *Overdose*). Thus, the use of *BECADEXAMIN* is contraindicated during the treatment with retinoids (see 4.3 *Contraindications*).

Oral contraceptives
Oral contraceptives may increase vitamin A plasma concentration.

Serum concentration of vitamin B_6, vitamin B_{12} and folic acid may be decreased by use of oral contraceptives.

Large supplements of vitamin C have been reported to increase serum ethinylestradiol concentrations in women taking oral contraceptives, but a further study showed no effect on either ethinylestradiol or levonorgestrel.

Levodopa
BECADEXAMIN contains vitamin B_6 which reduces the effects of levodopa, but this does not occur if a dopa decarboxylase inhibitor is also given.

Altretamine
BECADEXAMIN contains vitamin B_6 which reduces the activity of altretamine.

Lithium
The effects of iodine and iodides on the thyroid may be altered by other compounds including lithium.

Antiepileptics
Vitamin B_6 and folic acid has been reported to decrease serum concentrations of phenobarbital and phenytoin.

Some antiepileptics (e.g. carbamazepine, phenobarbital, phenytoin, and primidone) may increase vitamin D requirements.

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.

Concomitant nicotinamide and carbamazepine may decrease carbamazepine clearance.

Hydralazine
Hydralazine may increase the requirements for pyridoxine.

Omeprazole
Omeprazole has been reported to impair the bioavailability of vitamin B_{12} and dietary vitamin C.

Anticoagulants
As *BECADEXAMIN* contains vitamin E, caution should be used during concomitant administration of anticoagulants (dicoumarol, warfarin, indanediones) due to the risk of their efficacy reduction, hypoprothrombinaemia and bleeding. During prolonged administration of vitamin E, the prothrombin time should be monitored on a regular basis.

Cyclosporine
Vitamin E may increase the absorption of cyclosporine.

Calcium, vitamin D
There is an increased risk of hypercalcaemia if vitamin D is given with calcium. Vitamin D increases the gastrointestinal absorption of calcium. Plasma-calcium concentrations should be monitored in such situations.

Fluoride
As *BECADEXAMIN* contains calcium, it reduces the absorption of fluoride; therefore doses should be separated by at least 3 hours.

Phosphates
As *BECADEXAMIN* contains vitamin D, there is an increased risk of hypercalcaemia if it is given with phosphate. Plasma-calcium concentrations should be monitored in such situations.

Phosphorus-containing preparations may reduce the absorption of zinc.

Iron supplements
The absorption of zinc may be reduced by additionally taken iron supplements.

Calcium in *BECADEXAMIN* may reduce iron absorption when administered concomitantly with iron supplements. Oral iron preparations should not therefore be taken within 1 hour before or 2 hours after taking *BECADEXAMIN*.

Zinc supplements
Additionally, taken zinc supplements reduce the absorption of copper.

Prolonged use of high doses of zinc supplements, leads to copper deficiency with associated sideroblastic anaemia and neutropenia.

Vitamin C
As *BECADEXAMIN* contains vitamin C, it may increase the absorption of iron in iron-deficiency states.

Alcohol
Alcohol enhances the toxic effect of vitamin A and may produce folate deficiency states.

Other
Absorption of vitamin B_{12} from the gastrointestinal tract may be reduced by aminosalicylic acid, histamine H_2-antagonists, and colchicine. Aluminium, and magnesium salts may decrease the absorption of fluoride.

4.6 Use in Special Populations
Patients over the age of 45 years or with nodular goiter are especially susceptible to hyperthyroidism when given iodine supplementation. Reduced doses should therefore be used and supplementation with iodised oil may not be appropriate.

Fertility
There are no relevant data available.

Pregnancy
BECADEXAMIN should be used by pregnant women only after consultation with a physician.

Lactation
BECADEXAMIN should be used by lactating women only after consultation with a physician.

4.7 Effects on Ability to Drive and Use Machines

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

4.8 Undesirable Effects

The following adverse events have been reported with use of ingredients of *BECADEXAMIN*.

The frequency of most of these events cannot be estimated from the available 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)*, anaphylactic reaction.

Gastrointestinal disorders

Not Known: Abdominal pain, nausea, vomiting, diarrhoea, constipation, gastrointestinal disturbances, black faeces.

Psychiatric disorders

Not Known: Sleep disturbances.

Nervous system disorders

Not Known: Headache, dizziness

Skin and subcutaneous tissue disorders

Not Known: Rash, dermatitis acneiform and dermatitis bullous

Metabolic disorders

Very Rare: Diabetogenic effects

4.9 Overdose

Overdose of *BECADEXAMIN* can lead to the following symptoms and signs.

Symptoms and signs

Symptoms include: gastrointestinal disturbances (abdominal pain, nausea, vomiting, diarrhoea, constipation, taste disturbances, thirst), cardiac arrhythmias (tachycardia, bradycardia), hypotension, cardiac arrest, renal impairment, polyuria, nocturia, muscle weakness, headache, drowsiness, dizziness/vertigo, irritability, sweating, lassitude, somnolence, confusion, shock, coma, thirst, elevations in liver tests and liver damage, including jaundice and parenchymal liver cell injury.

Treatment

The treatment consists of its withdrawal and symptomatic treatment, if necessary.
Further management should be as clinically indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of action and Pharmacodynamic Effects

BECADEXAMIN contains active substances with synergistic, therapeutic actions, necessary for maintenance and/or improvement of functional activities of the body. Vitamins, their precursors, minerals and trace elements are included to treat deficiencies. Many of those act as co-factors for various metabolic functions.

Vitamin A
Retinol is an essential nutrient needed in small amounts by humans for the normal functioning of the visual system, growth and development and maintenance of epithelial cellular integrity, immune function and reproduction.

Vitamin D (cholecalciferol)
Vitamin D is required to maintain normal blood levels of calcium and phosphate, which are in turn needed for the normal mineralization of bone, muscle contraction, nerve conduction and general cellular function in all cells of the body.

Vitamin E (α-tocopherol acetate)
Vitamin E is the major lipid-soluble antioxidant in the cell antioxidant defence system acts and maintains the integrity of the vascular endothelium.

Vitamin B_1 (thiamine mononitrate)
Vitamin B_1 is an essential co-enzyme in oxidative metabolism of α-ketoacids and increases the activity of acetylcholine in nerve endings.

Vitamin B_2 (riboflavin)
Vitamin B_2 is an essential component in function of certain co-enzymes important for energy production taking part in numerous oxidation and reduction reactions. It has also an important role in maintaining a healthy skin.

Nicotinamide
Nicotinamide is involved in a large number of processes such as production of energy, synthesis of fatty acids, cholesterol, steroids, signal transduction and the maintenance of integrity of genome.

D-Panthenol
D-Panthenol (Dexpanthenol) is the synthetic alcohol form of pantothenic acid. It is converted to pantothenic acid in the body and therefore, can be considered a provitamin form of panothenic acid. Pantothenic acid is a precursor of co-enzyme A, necessary for energy production, involved in fatty acid metabolism, formation of acetylcholine and improvement of epithelization and wound healing. It is also necessary for folic acid and carbohydrate metabolism.

Vitamin B_6 (pyridoxine hydrochloride)
It takes part in formation of some important co-enzymes involved in protein metabolism and HEM biosynthesis. As a coenzyme it functions in metabolism of amino acids, glycogen and sphingoid bases.

Vitamin C (ascorbic acid)
Vitamin C is an electron donor (reducing agent or antioxidant) for 11 enzymes. It has a role in hydroxylation of certain compounds. It helps in maintenance of intracellular skeleton of cartilages, bones and teeth. It is essential in maintenance of capillary wall integrity and regulation of capillary permeability. Vitamin C promotes absorption of soluble non-haem iron.

Folic acid
It is essential for erythropoiesis, maturation of red blood cells and biosynthesis of the DNA.

Vitamin B_{12} (cyanocobalamin)
It is essential for erythropoiesis, formation of myelin sheet and synthesis of the DNA.

Calcium
It activates certain enzymes. It maintains the normal excitability of the myocardium and nerves and helps in maintenance of capillary wall integrity. It is essential in the structure of bones and teeth, for muscular contraction and many metabolic processes.

Copper
It is essential for synthesis of hemoglobin, formation of bone and myelin, for the activity of certain enzymes, such as cytochrome oxidases (tissue oxidation).

Manganese
It is a co-factor in many enzyme reactions, which involve phosphorylation and synthesis of cholesterol and fatty acids.

Zinc
Zinc is an essential component of a large number (> 300) of enzymes participating in the synthesis and degradation of carbohydrates, lipids, proteins, and nucleic acids as well as in the metabolism of other micronutrients. Zinc plays a major role in the immune system. It

also acts as an antioxidant. It is important for normal growth, wound healing and sexual maturation, for crystallization and release of insulin (the pancreas of diabetic individuals contains only half of the normal quantity of zinc).

Iodine
It has a role in the synthesis of thyroid hormones.

Magnesium
Magnesium functions as a co-factor of many enzymes involved in energy metabolism, protein synthesis, RNA and DNA synthesis, maintenance of the electrical potential of nervous tissues, cell membrane stabilizing action and muscle contraction.

5.2 Pharmacodynamic Properties

Pharmacotherapeutic group: Multivitamins and other minerals, including combinations, ATC Code A11AA03.

5.3 Pharmacokinetic Properties

There are no relevant data available.

5.4 Clinical Studies

There are no relevant data available.

6. NONCLINICAL PROPERTIES

There are no relevant data available.

7. DESCRITPTION

Capsules for oral administration.

Each Soft Gelatin capsule contains:

Vitamin A (as Vitamin A Concentrate Oil IP)	5000 IU
Vitamin D_3 (Cholecalciferol IP)	400 IU
Vitamin E (Tocopheryl Acetate IP)	15 mg
Vitamin B_1 IP	5 mg
Vitamin B_2 IP	5 mg
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Vitamin B_{12} IP	5 mcg
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Copper Sulfate Pentahydrate BP	0.1 mg
Manganese Sulfate Monohydrate BP	0.01 mg
Zinc Sulphate Monohydrate IP	28.7 mg (equivalent to 10.4 mg of elemental Zinc)

Potassium Iodide IP	0.025 mg
Light Magnesium Oxide IP	0.15 mg

(Appropriate overages added)
Excipients q.s.
Approved colours used in empty gelatin capsule shell.

List of Excipients
Lecithin Soyabean, Partially Hydrogenated Vegetable Oil, Yellow Beeswax, Arachis oil. Gelatin mass for soft gelatin capsule contains Gelatin, Glycerin, Purified water, Ethyl Vanillin, Methyl Hydroxybenzoate, Ethyl Hydroxybenzoate, Propyl Hydroxybenzoate. Capsule shell contains colours Sunset Yellow FCF, Brilliant Blue FCF, Erythrosine, Ponceau 4R and 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

Soft gelatin capsules in amber glass bottle or in HDPE bottle.

8.4 Storage and Handling Instructions

Store at temperature not exceeding 30^0 C protected from direct sunlight.

Keep out of reach of children.

9. PATIENT COUNSELLING INFORMATION

Registered Medical Practitioners may counsel their patients (and/or patient's caregiver as applicable) about the special warnings and precautions for use, drug interactions, undesirable effects, and any relevant contra-indications of *BECADEXAMIN*. Patients (and/or the 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

22-MAR-2024

Version: BEC/PI/IN/2024/01

Adapted from:

- Theragran M NCDS version 05 dated 21 January 2020
- PDR for Nutritional Supplements. 2nd edition.