Multivitamin with Vitamin A and Vitamin D3 Liquid

BECOSULES® + SYRUP

1. GENERIC NAME

Multivitamin with Vitamin A and Vitamin D3 Liquid

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml (1 teaspoonful) contains:

Vitamin A Concentrate Oil I.P. (as Palmitate)	2500 IU
Cholecalciferol I.P.	200 IU
Thiamine Hydrochloride I.P.	2 mg
Riboflavin Sodium Phosphate I.P.	2.54 mg
Pyridoxine Hydrochloride I.P.	1 mg
Niacinamide I.P.	20 mg
D-Panthenol I.P.	5 mg
Ascorbic Acid I.P.	50 mg

For Pediatric Use

List of Excipients

Citric Acid (monohydrate) IP
Sodium Bicarbonate IP (anhydrous)
Sodium Benzoate IP
Polysorbate 80 IP
Oil Orange Concentrate 16X
Glycerin IP
Sorbitol Solution (70%) (Non-crystallizing) IP
Butylated Hydroxy Anisole BP
Butylated Hydroxy Toluene IP
Purified Water IP

®Trademark Owner: Pfizer Products Inc. USA;
Licensed User: Pfizer Limited, India

3. DOSAGE FORM AND STRENGTH

Dosage Form - Oral Liquid
Strength - Refer Section 2

4. CLINICAL PARTICULARS

4.1 Therapeutic Indication

Becosules + Syrup is indicated in the treatment of patients with deficiencies of, or increased requirement for vitamins A, B complex, C and D. Such patients and conditions include:

- Decreased intake because of restricted or unbalanced diet as in anorexia, diabetes mellitus and obesity, and insufficient sunlight exposure.
- Reduced availability during treatment with antimicrobials which alter normal intestinal flora, and anticonvulsants and glucocorticoids which alter vitamin D metabolism, in prolonged diarrhea and in chronic gastrointestinal disorders.
- Increased requirements due to increased metabolic rate as in fever and tissue wasting, e.g. febrile illness, acute or chronic infections, surgery, burns and fractures.
- Stomatitis, glossitis, cheilosis, paraesthesias, neuralgia and dermatitis.

4.2 Posology and Method of Administration

For children from 1-3 years - 1.25 ml, 4-9 years - 2.5 ml; and 10-13 years - 5 ml or as directed by physician.

4.3 Contraindications

Hypersensitivity to any of the ingredients of Becosules + Syrup

4.4 Special Warnings and Precautions for Use

The use of Becosules + Syrup in patients with deficiency or increased requirement of vitamins A, B complex, C and D should be accompanied by specific therapy for the primary illness.

Treatment with Becosules + Syrup should be continued only until the deficiency is corrected or the need for supplementation exists.

Pyridoxine in Becosules + Syrup may reduce the therapeutic effects of levodopa in Parkinson's disease.

Riboflavin in Becosules + Syrup may color the urine yellow.

During treatment with Becosules + Syrup, the urine may give a false positive result for sugar by Benedict's test because of the presence of ascorbic acid. Therefore, a test-not affected by ascorbic acid-should be used.

Excessive intake of vitamins A and D can lead to hypervitaminosis A and D, respectively.

Keep out of reach of (young) children.

Do not exceed recommended daily dose/amount.

4.5 Drugs Interactions

No major interactions with any concomitant medications. However, patients on steroids and antibiotics may have a reduced absorption of vitamin D and B complex within the formulation.

4.6 Use in Special Populations

NA

4.7 Effects on Ability to Drive and use Machines

NA

4.8 Undesirable Effects

Some patients may experience discoloration of urine.

4.9 Overdose

Excessive amounts over long periods can lead to toxicity- hypervitaminosis A and D.

Hypervitaminosis A may be acute or chronic. Acute cases are characterized by exaggeration of normal physiological and biochemical actions. Features include dizziness, headache, lassitude, irritability, pain in abdomen, nausea, visual disturbances, pruritus and excoriation of skin. Chronic cases are manifested by low grade fever, alopecia, dry fissured lip, ache in bones and joints, hyperostosis,

anorexia, weight loss, hepatosplenomegaly and papilloedema and pseudotumor cerebri. Management is by stopping the vitamin preparation.

Most symptoms of hypervitaminosis D occur because of secondary hypercalcaemia with increased bone resorption and hypercalciuria. They include: polyuria, polydipsia, vomiting, anorexia, lethargy, dehydration, constipation, hypertension, tetany, seizures, dental enamel hypoplasia, focal pulp calcification, nephrolithiasis and nephrocalcinosis.

In case of overdose, discontinue the use of Becosules + Syrup and contact your doctor or healthcare professional immediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Mechanism of Action

Vitamin A

Vitamin A is the name of a group of fat-soluble retinoids, including retinol, retinal, and retinyl esters. Refer to Section 5.2 for additional details.

Vitamin A deficiency is a major public health problem worldwide. It is the leading preventable cause of blindness among children in developing nations. The earliest evidence of vitamin A deficiency is impaired dark adaptation or night blindness.

Vitamin A deficiency also places children at a heightened risk for infectious disease.

Cholecalciferol

Vitamin D is a fat-soluble vitamin that is naturally present in very few foods. Refer to Section 5.2 for additional details.

Severe vitamin D deficiency in infants and children results in the failure of bone to mineralize, leading to a condition known as rickets. Rapidly growing bones are most severely affected by rickets. The growth plates of bones continue to enlarge, but in the absence of adequate mineralization, weight-bearing limbs (arms and legs) become bowed.

Vitamin B1

Thiamin (or thiamine) is one of the water-soluble B vitamins. It is also known as vitamin B1. Refer to Section 5.2 for additional details.

Early detection of subclinical thiamine deficiency is a difficult task, as symptoms may be vague and nonspecific, such as frequent headaches, fatigue, irritability, abdominal discomfort, and decline in the growth rate of children.

Vitamin B2

Riboflavin (also known as vitamin B2) is one of the B vitamins, which are all water soluble. Riboflavin is naturally present in some foods, added to some food products, and available as a dietary supplement. Refer to Section 5.2 for additional details.

The signs and symptoms of riboflavin deficiency (also known as ariboflavinosis) include skin disorders, hyperemia (excess blood) and edema of the mouth and throat, angular stomatitis (lesions at the corners of the mouth), cheilosis (swollen, cracked lips), hair loss, sore throat, itchy and red eyes. Severe riboflavin deficiency can impair the metabolism of other nutrients, especially other B vitamins, through diminished levels of flavin coenzymes.

Pyridoxine

Vitamin B6, also called pyridoxine, is one of eight B vitamins. Refer to Section 5.2 for additional details.
B complex vitamins are needed for healthy skin, hair, eyes, and liver. They also help the nervous system function properly.

It is rare to have a significant deficiency of B6, although studies indicate many people may be mildly deficient, especially children and the elderly.

Symptoms of serious deficiency include:

- Muscle weakness
- Nervousness
- Irritability
- Difficulty concentrating

Niacinamide

Niacin is chemically synonymous with nicotinic acid although the term is also used for its amide (nicotinamide). Nicotinamide is the other form of the vitamin, which does not have the pharmacologic action of the acid that is administered at high doses to lower blood lipids. Refer to Section 5.2 for additional details.

Niacin (nicotinic acid) deficiency classically results in pellagra.

Panthenol

Pantothenic acid is a component of CoA, a cofactor that carries acyl groups for many enzymatic processes, and of phosphopantetheine within acyl carrier protein, a component of the fatty acid synthase complex. Refer to Section 5.2 for additional details.

Vitamin B5 deficiency is rare, but may include symptoms such as fatigue, insomnia, irritability, vomiting, stomach pains.

Ascorbic acid

Vitamin C, also known as L-ascorbic acid, is a water-soluble vitamin that is naturally present in some foods, added to others, and available as a dietary supplement. Humans, unlike most animals, are unable to synthesize vitamin C endogenously, so it is an essential dietary component. Refer to Section 5.2 for additional details.

Insufficient vitamin C intake causes scurvy, which is characterized by fatigue or lassitude, widespread connective tissue weakness, and capillary fragility.

5.2 Pharmacodynamic Properties

Vitamin A - Vitamin A is involved in immune function, vision, reproduction, and cellular transmission. Vitamin A is critical for vision as an essential component of rhodopsin, a protein that absorbs light in the retinal receptors, and because it supports the normal differentiation and functioning of the conjunctival membranes and cornea. Vitamin A also supports cell growth and differentiation, playing a critical role in the normal formation and maintenance of the heart, lungs, kidneys, and other organs.

Cholecalciferol - Vitamin D promotes calcium absorption in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal mineralization of bone and to prevent hypocalcemic tetany. It is also needed for bone growth and bone remodeling by osteoblasts and osteoclasts. Without sufficient vitamin D, bones can become thin, brittle, or misshapen. Vitamin D has other roles in the body, including modulation of cell growth, neuromuscular and immune function, and reduction of inflammation.

Vitamin B1 - This vitamin plays a critical role in energy metabolism and, therefore, in the growth, development, and function of cells

Vitamin B2 - This vitamin is an essential component of two major coenzymes, flavin mononucleotide (FMN; also known as riboflavin-5'-phosphate) and flavin adenine

dinucleotide (FAD). These coenzymes play major roles in energy production; cellular function, growth, and development; and metabolism of fats, drugs, and steroids.

Pyridoxine -. B complex vitamins are needed for healthy skin, hair, eyes, and liver. They also help the nervous system function properly. Vitamin B6 helps the body make several neurotransmitters – chemicals that carry signals from one nerve cell to another. It is needed for normal brain development and function, and helps the body make the hormones serotonin and norepinephrine, which influence mood, and melatonin, which helps regulate the body clock.

Niacinamide - It is the amide form that exists within the redox-active co-enzymes, nicotinamide adenine dinucleotide (NAD) and its phosphate (NADP), which function in dehydrogenase-reductase systems requiring transfer of a hydride ion. NAD is also required for non-redox adenosine diphosphate–ribose transfer reactions involved in DNA repair and calcium mobilisation. NAD functions in intracellular respiration and with enzymes involved in the oxidation of fuel substrates. NADP functions in reductive biosyntheses such as fatty acid and steroid syntheses and in the oxidation of glucose-6-phosphate to ribose-5-phosphate in the pentose phosphate pathway.

Panthenol - Pantothenate is most especially involved in fatty acid metabolism but has a wide-ranging function as a prosthetic group that adds specificity to binding with appropriate enzymes.

Ascorbic acid -Vitamin C is required for the biosynthesis of collagen, L-carnitine, and certain neurotransmitters; vitamin C is also involved in protein metabolism. Collagen is an essential component of connective tissue, which plays a vital role in wound healing.Vitamin C is also an important physiological antioxidant and has been shown to regenerate other antioxidants within the body, including alpha-tocopherol (vitamin E).In addition to its biosynthetic and antioxidant functions, vitamin C plays an important role in immune function and improves the absorption of nonheme iron, the form of iron present in plant-based foods.

5.3 Pharmacokinetic Properties

All B vitamins and Vitamin C are water-soluble, meaning that the body does not store them. These are meagerly stored: excess is excreted with little chance of toxicity. They act as cofactors for specific enzymes of intermediary.

Vitamin B1 - After conversion in the body to Thiamine pyrophosphate, it acts as a coenzyme in carbohydrate metabolism. Physiological amounts are absorbed by active transport. When large doses are given orally, some passive diffusion also occurs. Limited amounts are stored in tissues. About 1 mg/day is degraded in the body, excess is rapidly excreted in urine.

Vitamin B2 - Well absorbed by active transport and phosphorylated in the intestine. Riboflavin phosphate (Flavin mononucleotide: FMN) is formed in other tissues as well. Body does not significantly store riboflavin; larger doses are excreted unchanged in urine. Thiamine and riboflavin are both synthesized by colonic bacteria but this does not become available to the host.

Pyridoxine - Pyridoxine, Pyriodoxal and Pyridoxamine are related naturally occurring pyridine compounds that have vit B6 activity. All three forms of the vitamin are well absorbed from the intestine. They are oxidized in the body and excreted as pyridoxic acid. Little is stored.

Niacinamide - Niacin refers to Nicotinic acid as well as Nicotinamide—pyridine compounds. Niacin is completely absorbed from gastrointestinal tract. Physiological amounts are metabolized in the body, while large doses are excreted unchanged in urine. Modest amounts are stored in liver. Nicotinic acid is readily converted to its amide which is a component of the coenzyme Nicotinamideadenine-dinucleotide (NAD) and its phosphate (NADP) involved in oxidation-reduction reactions.

Panthenol - It is quickly absorbed and excreted unchanged in urine with little storage.

Ascorbic Acid - Ascorbic acid is nearly completely absorbed from g.i.t. and widely distributed extra- and intracellularly. Plasma concentration and total body store of vit C is related to daily intake. The usual 60 mg/day intake results in about 0.8 mg/dl in plasma and 1.5 g in the body as a whole. Increasing proportions are excreted in urine with higher intakes. Body is not able to store more than 2.5 g. It is partly oxidized to active (dehydroascorbic acid) and inactive (oxalic acid) metabolites.

Vitamins A, D are fat soluble vitamins. These are stored in the body for prolonged periods and are liable to cause cumulative toxicity after regular ingestion of large amounts. Some interact with specific cellular receptors analogous to hormones.

Vitamin A - Man on normal diet gets half of his vit A as retinol esters and half from carotenoids. Retinyl palmitate, the chief retinyl ester in diet, is hydrolysed in intestines to retinol which is absorbed by carrier transport and reesterified. Aided by bile, it passes into lacteals. Absorption is normally complete, but not in steatorrhoea, bile deficiency and from protein poor diet. Retinol ester circulates in chylomicrons and is stored in liver cells. Free retinol released by hepatocytes combines with retinol binding protein (RBP a plasma globulin) and is transported to the target cells. On entering them, it gets bound to the cellular retinol binding protein (CRBP). Small amount is conjugated with glucuronic acid, excreted in bile, undergoes enterohepatic circulation. Minute quantities of water soluble metabolites are excreted in urine and faeces. In contrast to retinol, only 30% of dietary β carotene is absorbed. It is split

into two molecules of retinal in the intestinal wall; only half of this is reduced to retinol and utilized.

Cholecalciferol(Vit D3) - Vit D is well absorbed from the intestines in the presence of bile salts, mainly through lymphatics. Absorption of the D3 form is somewhat better than that of D2 (calciferol). Malabsorption and steatorrhoea interfere with its absorption. In the circulation, it is bound to a specific α globulin and is stored in the body, mostly in adipose tissues, for many months. It is hydroxylated in the liver to active and inactive metabolites. The $t_{½}$ of different forms varies from 1–18 days: Metabolites of vit D are excreted mainly in bile.

6. NONCLINICAL PROPERTIES

6.1 Animal Toxicology or Pharmacology

No data available.

7. DESCRIPTION

A clear golden yellow to amber coloured syrupy liquid free from foreign matter.

8. PHARMACEUTICAL PARTICULARS

8.1 Incompatibilities

NA

8.2 Shelf-life

12 Months

8.3 Packaging Information

200 ml amber colored PET bottle

8.4 Storage and Handling Instructions

Store below 25°C. Protect from light.

Instructions for Use and Handling

Replace cap securely.

9. PATIENT COUNSELLING INFORMATION

The use of Becosules + Syrup in patients with deficiency or increased requirement of vitamins A, B complex, C and D should be accompanied by specific therapy for the primary illness. Patients should be counseled that treatment with Becosules + Syrup should be continued only until the deficiency is corrected or the need for supplementation exists. Patients should be cautioned that Pyridoxine in Becosules + Syrup may reduce the therapeutic effects of levodopa in Parkinson's disease. Riboflavin in Becosules + Syrup may color the urine yellow. During treatment with Becosules + Syrup, the urine may give a false positive result for sugar by Benedict's test because of the presence of ascorbic acid. Excessive intake of vitamins A and D can lead to hypervitaminosis A and D, respectively. Patients on steroids and antibiotics may have a reduced absorption of vitamin D and B complex within the formulation. Keep out of reach of (young) children. Do not exceed recommended daily dose/amount. In case of overdose, discontinue the use of Becosules + Syrup and contact your doctor or healthcare professional immediately.

10. DETAILS OF MANUFACTURER

Manufactured by:
Pfizer Limited at C-4,13, MIDC, Functional Electronic Estate, Bhosari, Pune - 411026, India.

11. DETAILS OF PERMISSION OR LICENSE NUMBER WITH DATE

Manufacturing Licence No.*: 28A-PD/198-A dated 06 Feb 2006

*The manufacturing license is renewed every 5 years as per Indian regulations.

12. DATE OF REVISION

August 2023