Legal Category

OTC

SmPC

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

KRISTYMIN Syrup

Amino Acids & Multivitamin Syrup

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 15 ml (one tablespoonful) contains:

L-Leucine USP……...18.3 mg

L-isoleucine USP…….5.9 mg

L-Lysine hydrochloride USP…….25mg

L-Phenylalanine USP……..5 mg

L-tryptophan USP……...5 mg

L-valine USP ……...6.7 mg

Thiamine hydrochloride BP……5 mg

Riboflavin BP…….3 mg

Pyridoxine hydrochloride BP……...1.5 mg

Nicotinamide BP……...25 mg

Calcium pantothenate BP……5 mg

Cyanocobalamin BP……...2.5 mcg

Folic acid BP……..0.75 mg

Ascorbic acid BP……...40 mg

Vitamin A BP……2500 I.U.

Cholecalciferol BP……..200 I.U.

Alpha tocopherol acetate BP…….7.5 I.U.

Overages of Vitamins added to compensate loss on storage.

3. PHARMACEUTICAL FORM

Oral Liquid

Brown colored syrup with éclair Chocolate flavor.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

KRISTYMIN Syrup is used as a nutritional supplement that is essential in children for growth, mental development, alertness, and general good health. In adults, it helps to cope with stress, strengthens immune system and quickens recovery from illness. It aids in the treatment of conditions associated with deficiency of certain B-complex vitamins, minerals, and amino acids, such as severe infections, degenerative diseases, endocrine dysfunction, surgical procedures, injuries, burns, old age, beriberi, riboflavinosis or pellagra.

4.2 Posology and method of administration

Do not use it if the cap seal on the bottle is broken when purchased. Keep the bottle tightly used after each use. Please read the enclosed leaflet carefully before each use.

Adults: 15 ml twice daily or as directed by the physician.

Shake well before each use.

Method of Administration

For oral administration

4.3 Contraindications

Contraindicated in patients known to be hypersensitive to any of its components and in patients with hypervitaminosis.

4.4 Special warnings and precautions for use

Multivitamins are not recommended for the treatment of specific deficiencies of vitamin and minerals. While taking the multivitamin, both protein and energy are also required to provide complete nutrition in the daily diet. No other vitamin, mineral or supplements with or without vitamin A should be taken with the preparation expect under medical supervision.

Do not take on an empty stomach. Do not exceed the stated dose. Keep out of reach children. If symptoms persist, consult your doctor.

4.5 Interaction with other medicinal products and other forms of interaction

The pyridoxine chloride may reduce the effectiveness of levodopa & folic acid can reduce the plasma concentration of phenytoin.

4.6 Pregnancy and lactation

KRISTYMIN SYRUP may be administered during pregnancy and lactation at the recommendation of the physician.

4.7 Effects on ability to drive and use machines.

None Known

4.8 Undesirable effects

Generally multivitamin and multimineral are well tolerated by the body. Sometimes, reactions could occur, but they disappear rapidly upon regular use.

Ascorbic acid (C), Nicotinamide, pyridoxine (B_6), Riboflavin (B_2) & Thiamine (B_1)

These water-soluble vitamins are generally nontoxic compounds with a wild margin of safety, the excess amounts being rapidly excreted in the urine.

4.9 Overdose

Seek emergency medical attention. Most reported symptoms of Vitamin & amino acid overdose include nausea and vomiting.

Symptoms and signs

KRISTYMIN SYRUP contains levels of vitamins which present little risk in overdose.

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5. Pharmacological properties

5.1 Pharmacodynamic properties

L-Leucine:

An essential amino acid. Leucine helps with the regulation of blood-sugar levels, the growth and repair of muscle tissue (such as bones, skin, and muscles), growth hormone production, wound healing as well as energy regulation. It can assist in preventing the breakdown of muscle proteins that sometimes occur after trauma or severe stress. It may also be beneficial for individuals with phenylketonuria - a condition in which the body cannot metabolize the amino acid phenylalanine.

L-isoleucine:

They provide ingredients for the manufacturing of other essential biochemical components in the body, some of which are utilized to produce energy, stimulants to the upper brain and helping you to be more alert.

L-Lysine hydrochloride:

Ensures the adequate absorption of calcium; helps form collagen (which makes up bone cartilage & connective tissues); aids in the production of antibodies, hormones & enzymes. Recent studies have shown that Lysine may be effective against herpes by improving the balance of nutrients that reduce viral growth. A deficiency may result in tiredness, inability to concentrate, irritability, bloodshot eyes, retarded growth, hair loss, anemia & reproductive problems.

L-Phenylalanine:

Used by the brain to produce Norepinephrine, a chemical that transmits signals between nerve cells and the brain; keeps you awake and alert; reduces hunger pains; functions as an antidepressant and helps improve memory.

L-Tryptophan:

Tryptophan is critical to produce the body's proteins, enzymes, and muscle tissue. It is also essential to produce niacin, the synthesis of the neurotransmitter serotonin and melatonin. Tryptophan supplements can be used as natural relaxants to help relieve insomnia. Tryptophan can also reduce anxiety and depression and has been shown to reduce the intensity of migraine headaches. Other promising indications include the relief of chronic pain, reduction of impulsivity or mania and the treatment of obsessive or compulsive disorders. Tryptophan also appears to help the immune system and can reduce the risk of cardiac spasms. Tryptophan deficiencies may lead to coronary artery spasms. Tryptophan is used as an essential nutrient in infant formulas and intravenous feeding. Tryptophan is marketed as a prescription drug (Tryptan) for those who do not seem to respond well to conventional antidepressants. It may also be used to treat those afflicted with seasonal affective disorder (a winter-onset depression). Tryptopan serves as the precursor for the synthesis of serotonin (5-hydroxytryptamine, 5-HT) and melatonin (N-acetyl-5-methoxytryptamine).

L-valine:

L-valine is a branched-chain essential amino acid (BCAA) that has stimulant activity. It promotes muscle growth and tissue repair. It is a precursor in the penicillin biosynthetic pathway. Valine is one of three branched-chain amino acids (the others are leucine and isoleucine) that enhance energy, increase endurance, and aid in muscle tissue recovery and repair. This group also lowers elevated blood sugar levels and increases growth hormone production. Supplemental valine should always be combined with isoleucine and leucine at a respective milligram ratio of 2:1:2. It is an essential amino acid found in proteins; important for optimal growth in infants and for growth in children and nitrogen balance in adults. The lack of L-valine may influence the growth of the body, cause neuropathic obstacle, anemia. It has wide applications in the field of pharmaceutical and food industry.

Thiamine:

Thiamine (as the coenzyme, thiamine pyrophosphate) is associated with carbohydrate metabolism. Thiamine pyrophosphate also acts as a co-enzyme in the direct oxidative pathway of glucose metabolism. In thiamine deficiency, pyruvic and lactic acids accumulate in the tissues. The pyruvate ion is involved in the biosynthesis of acetylcholine via its conversion to acetyl co-enzyme A through a thiamine-dependent process. In thiamine deficiency, therefore, there are effects on the central nervous system due either to the effect on acetylcholine synthesis or to the lactate and pyruvate accumulation. Deficiency of thiamine results in fatigue, anorexia, gastro- intestinal disturbances, tachycardia, irritability, and neurological symptoms. Gross deficiency of thiamine (and other Vitamin B group factors) leads to the condition beri-beri.

Riboflavin:

Riboflavin is phosphorylated to flavine mononucleotide and flavine adenine dinucleotide which act as co-enzymes in the respiratory chain and in oxidative phosphorylation. Riboflavin deficiency presents ocular symptoms, as well as lesions on the lips and at angles of the mouth.

Pyridoxine HCL:

Pyridoxine, once absorbed, is rapidly converted to the co-enzymes pyridoxal phosphate and pyridoxamine phosphate which play an essential role in protein metabolism. Convulsions and hypochromic anaemia have occurred in infants deficient in pyridoxine. B-complex Vitamin. The vitamin B-complex comprises a group of

water-soluble factors more or less closely associated in their natural occurrence. It is known that nearly every vitamin of the B-complex forms part of a co-enzyme essential for the metabolism of protein, carbohydrate, or fatty acid.

Nicotinamide:

The biochemical functions of nicotinamide as NAD and NADP (nicotinamide adenine dinucleotide phosphate) include the degradation and synthesis of fatty acids, carbohydrates and amino acids as well as hydrogen transfer. Deficiency produces pellagra and mental neurological changes.

Calcium pantothenate:

Pantothenic acid is used in the synthesis of coenzyme A (CoA). CoA is thought to act as a carrier molecule, allowing the entry of acyl groups into cells. This is of critical importance as these acyl groups are used as substrates in the tricarboxylic acid cycle to generate energy and in the synthesis of fatty acids, cholesterol, and acetylcholine. Additionally, CoA is part of acyl carrier protein (ACP), which is required in the synthesis of fatty acids in addition to CoAs use as a substrate.

Pantothenic acid in the form of CoA is also required for acylation and acetylation, which, for example, are involved in signal transduction and enzyme activation and deactivation, respectively.

Since pantothenic acid participates in a wide array of key biological roles, it may have numerous wide-ranging effects.

Cyanocobalamin:

Vitamin B12 is present in the body mainly as methyl cobalamin and as adenosyl cobalamin and hydroxocobalamin. These act as co-enzymes in the trans methylation of homocysteine to methionine; in the isomerization of methyl malonyl co-enzyme to succinyl co-enzyme and with folate in several metabolic pathways respectively. Deficiency of Vitamin B12 interferes with hemopoiesis and produces megaloblastic anaemia.

Folic acid:

Folic acid is a water-soluble B-complex vitamin found in foods such as liver, kidney, yeast, and leafy, green vegetables. Also known as folate or Vitamin B9, folic acid is an essential cofactor for enzymes involved in DNA and RNA synthesis. More specifically, folic acid is required by the body for the synthesis of purines, pyrimidines, and methionine before incorporation into DNA or protein. Folic acid is the precursor of tetrahydrofolic acid, which is involved as a cofactor for transformylation reactions in the biosynthesis of purines and thymidylates of nucleic acids. Impairment of thymidylate synthesis in patients with folic acid deficiency is thought to account for the defective deoxyribonucleic acid (DNA) synthesis that leads to megaloblast formation and megaloblastic and macrocytic anemias. Folic acid is particularly important during phases of rapid cell division, such as infancy, pregnancy, and erythropoiesis, and plays a protective factor in the development of cancer. As humans are unable to synthesize folic acid endogenously, diet and supplementation is necessary to prevent deficiencies. In order to function properly within the body, folic acid must first be reduced by the enzyme dihydrofolate reductase (DHFR) into the cofactors dihydrofolate (DHF) and tetrahydrofolate (THF). This important pathway, which is required for de novo synthesis of nucleic acids and amino acids, is disrupted by anti-metabolite therapies such as Methotrexate as they function as DHFR inhibitors to prevent DNA synthesis in rapidly dividing cells, and therefore prevent the formation of DHF and THF.

Ascorbic Acid:

Vitamin C cannot be synthesized by man therefore a dietary source is necessary. It acts as a cofactor in numerous biological processes including the hydroxylation of proline to hydroxyproline. In deficiency, the formation of collagen is, therefore, impaired. Ascorbic acid is important in the hydroxylation of dopamine to noradrenaline and in hydroxylation occurring in steroid synthesis in the adrenals. It is a reducing agent in tyrosine metabolism and by acting as an electron donor in the conversion of folic acid to tetrahydrofolic acid is indirectly involved in the synthesis of purine and thymine. Vitamin C is also necessary for the incorporation of iron into ferritin. Vitamin C increases the phagocytic function of leucocytes; it possesses anti-inflammatory activity, and it promotes wound healing. Deficiency can produce scurvy. Features include swollen inflamed gums, petechial hemorrhages, and subcutaneous bruising. The deficiency of collagen leads to the development of thin watery ground substances in which blood vessels are insecurely fixed and readily ruptured. The supportive components of bone and cartilage are also deficient causing bones to fracture easily and teeth to become loose. Anaemia commonly occurs probably due to Vitamin C role in iron metabolism.

Vitamin A:

Vitamin A plays an important role in the visual process. It is isomerized to the 11-cis isomer and subsequently bound to the opsin to form the photoreceptor for vision under subdued light. One of the earliest symptoms of deficiency is night blindness which may develop into the more serious condition xerophthalmia. Vitamin A also participates in the formation and maintenance of the integrity of epithelial tissues and mucous membranes. Deficiency may cause skin changes resulting in dry rough skin with lowered resistance to minor skin infections. Deficiency of Vitamin A, usually accompanied by protein-energy malnutrition, is linked with a frequency of infection and with defective immunological defense mechanisms.

Cholecalciferol:

Vitamin D is required for the absorption of calcium and phosphate from the gastro-intestinal tract and for their transport. Its involvement in the control of calcium metabolism and hence the normal calcification of bones is well documented. Deficiency of Vitamin D in children may result in the development of rickets.

Alpha tocopherol acetate:

Alpha tocopherol acetate of the eight separate variants of vitamin E, alpha-tocopherol is the predominant form of vitamin E in human and animal tissues, and it has the highest bioavailability. This is because the liver preferentially resecretes only alpha-tocopherol by way of the hepatic alpha-tocopherol transfer protein (alpha-TTP); the liver metabolizes and excretes all the other vitamin E variants, which is why blood and cellular concentrations of other forms of vitamin E other than alpha-tocopherol are ultimately lower.

Furthermore, the term alpha-tocopherol generally refers to a group of eight possible stereoisomers which is often called all-rac-tocopherol for being a racemic mixture of all eight stereoisomers, the eight stereoisomers, the RRR-alpha-tocopherol - or sometimes referred to as the d-alpha-tocopherol - stereoisomer is the naturally occurring form of alpha-tocopherol that is perhaps best recognized by the alpha-TTP, and has been reported to demonstrate approximately twice the systemic availability of all-rac-tocopherol .

As a result, often (but certainly not always) the discussion of vitamin E - at least within the context of using the vitamin for health-related indications - is generally in reference to the use of RRR- or d-alpha-tocopherol.

Pharmacokinetic properties:

L-Leucine:

Leucine metabolism occurs in many tissues in the human body; however, most dietary leucine is metabolized within the liver, adipose tissue, and muscle tissue. Adipose and muscle tissue use leucine in the formation of sterols and other compounds. Combined leucine use in these two tissues is seven times greater than in the liver.

L-isoleucine:

In healthy individuals, the plasma levels of ketoacids increase within 10 min after oral administration. Increases of up to 5-fold the baseline levels are achieved. Peak levels occur within 20-60 min, and after 90 min levels stabilize in the range of the base levels. Gastrointestinal absorption is thus very rapid.

L-Lysine hydrochloride:

Oral administration is the preferred route for lysine supplementation. Upon ingestion, it is absorbed from the lumen of the small intestine into the enterocytes via active transport and moves from the gut to the liver via portal circulation.

L-Phenylalanine:

Pharmacokinetics of phenylalanine or PEA have not been established. In research studies, phenylalanine and PEA have been well tolerated with very few adverse effects, and no effects of nausea, fatigue, sleep changes, or cardiovascular effects have been observed.

L-tryptophan:

The data obtained following the oral administration of L-tryptophan suggests that the total body clearance and apparent volume of distribution are saturable. The pharmacokinetics of tryptophan after intravenous administration of 5 g and 7.5 g were like those after the oral administration of 25 and 50 mg kg-1 (i.e., 1.75 g and 3.5 g).

L-valine:

quick oral absorption, high tissue permeability, wide distribution in the body. Long in vivo half-life owing to its high lipophilicity.

Thiamine:

Thiamine is absorbed from the gastro-intestinal tract and is widely distributed to most body tissues. Amounts more than the body’s requirements are not stored but excreted in the urine as unchanged thiamine or its metabolites.

Riboflavin:

Riboflavin is absorbed from the gastro-intestinal tract and in the circulation is bound to plasma proteins. It is widely distributed. Little is stored and excess amounts are excreted in the urine. In the body riboflavin is converted to flavine mononucleotide (FMN) and then to flavine adenine dinucleotide (FAD).

Pyridoxine:

Pyridoxine is absorbed from the gastro-intestinal tract and converted to the active pyridoxal phosphate which is bound to plasma proteins. It is excreted in the urine as 4-pyridoxic acid.

Nicotinamide:

Nicotinic acid is absorbed from the gastro-intestinal tract, is widely distributed in the body tissues and has a short half-life.

Calcium pantothenate:

Calcium pantothenate is easily absorbed in the intestine and is broken down, releasing pantothenic acid. Pantothenic acid is involved in carbohydrate and fat metabolism, stimulates the formation of corticosteroids, accelerates the regeneration processes. About 60% is excreted in the urine, partially in the feces.

Cyanocobalamin:

Cyanocobalamin is absorbed from the gastro-intestinal tract and is extensively bound to specific plasma proteins. A study labelled Vitamin B12 showed it was quickly taken up by the intestinal mucosa and held there for 2 - 3 hours. Peak concentrations in the blood and tissues did not occur until 8 - 12 hours after dosage with maximum concentrations in the liver within 24 hours. Cobalamins are stored in the liver, excreted in the bile, and undergo enterohepatic recycling. Part of a dose is excreted in the urine, most of it in the first eight hours.

Folic acid:

Well absorbed from the GI tract. Synthetic folic acid is almost 100% bioavailable following oral administration in fasting individuals; folate in food is about 50% bioavailable. Synthetic folic acid is 85–100% bioavailable following oral administration with a meal. Distributed into all body tissues including the CNS; stored mainly in the liver. Distributed into all body tissues including the CNS; stored mainly in the liver. Up to 90% of a dose in urine; small amounts in feces.

Ascorbic Acid:

Ascorbic acid is readily absorbed from the gastro-intestinal tract and is widely distributed in the body tissues. Ascorbic acid more than the body’s needs is rapidly eliminated in the urine and this elimination is usually accompanied by a mild diuresis.

Vitamin A:

Except when liver function is impaired, Vitamin A is readily absorbed. Retinol is emulsified by bile salts and phospholipids and absorbed in a micellar form. Part is conjugated with glucuronic acid in the kidney and part is metabolized in the liver and kidney, leaving 30 to 50% of the dose for storage in the liver. It is bound to a globulin in the blood. Metabolites of Vitamin A are excreted in the feces and the urine.

Cholecalciferol:

Cholecalciferol is absorbed from the gastro-intestinal tract into the circulation. In the liver, it is hydroxylated to 25-hydroxycholecalciferol, is subject to entero-hepatic circulation and is further hydroxylated to 1,25-dihydroxycholecalciferol in the renal tubule cells. Vitamin D metabolites are bound to specific plasma proteins.

Alpha tocopherol acetate:

The individual pharmacokinetic parameters were absorption rate constant, Ka1 = 0.29 +/- 0.02/h; the second absorption rate constant, Ka2 = 0.03 +/- 0.002/h; elimination half-life = 42.40 +/- 1.70/h; mean residence time = 46 +/- 0.92 h; and area under the curve = 290 +/- 10.77 micrograms/h per ml

5.2 Pharmacokinetic properties

The pharmacokinetics of the active substances would not be different from those naturally derived by food orally.

5.3 Pre-clinical Safety:

None Stated.

6. Pharmaceutical Particulars:

6.1 List of Excipients:

Sucrose, Sucrose, Sodium Methyl Paraben, Sodium Propyl Paraben, Sodium Benzoate, Citric acid Monohydrate, Bronopol BP, Arrow Gum Super, Disodium EDTA, Sodium Hydroxide, Acrysol-K-140, Sodium Metabisulphite, Butylated Hydroxy Anisole, Butylated Hydroxy Toluene, Saccharin sodium powder, Colour Caramel

6.2 Incompatibilities:

There are no significant incompatibilities with the product.

6.3 Shelf Life

3 Years.

6.4 Special Precautions for storage

Store below 30°C. Protect from direct sunlight.

6.4 Nature and contents of container

200 amber PET bottle provided with a measuring cup packed in a Carton along with the Pack Insert.

6.5 Special precautions for disposal and other handling

No Special requirement for disposal

Marketing Authorization Holder:

Krishat Pharma Industries Limited KM 15, Lagos-Ibadan Expressway, Ibadan, Oyo State, NIGERIA.

Email: info@krishatpharma.com

7. Marketing Authorization Number (s)

NA

8. Date of first Authorization /renewal of the authorization

NA

9. Date of revision of text

NA

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