Name of the medicinal product

Uptamin Capsules

2. Qualitative and quantitative composition

Each capsule contains:

Essential Amino Acids	
L-Leucine	18.3mg
L-Isoleucine	5.9mg
L-Lysine Hydrochloride	25mg
L-Phenylalanine	5mg
L-Threonine	4.2mg
L-Methionine	18.4mg
L-Tryptophan	5mg
L-Valine	6.7mg
Minerals	
Vitamin A (as synthetic retinol)	2500 I.U
Vitamin D (as Cholecalciferol)	200 I.U
Thiamine Hydrochloride	5mg
Riboflavin	3mg
Nicotinamide B.P	25mg
Pyridoxine Hydrochloride	1.5mg
Folic Acid	0.75mg
Calcium D-Pantothenate	5mg
Ascorbic Acid	25mg
Cyanocobalamin	2.5mcg
Alpha Tocopheryl Acetate	7.5 I.U

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Hard gelatin capsule.

4. Clinical particulars

4.1 Therapeutic indications

Uptamin is required in the following cases where amino acid and vitamin supplementation is necessary:

- Malnutrition
- Deficiency states
- Growing children
- Pregnancy and lactation
- Injury including burns, trauma and sepsis
- Convalescence from debilitating illness and infections
- Anorexia.
- Wasting diseases
- Low physical vigor due to fatigue and stress.
- Enhancement of natural resistance and recuperative power of the body

4.2 Posology and method of administration

Adults and the Elderly

One to 2 capsules daily, preferably taken one hour after meals. Do not exceed the stated dose. The capsule should be swallowed whole with water.

Children under 12 years of age

Uptamin Capsules are not recommended for this age group.

4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients.
- Stomach ulcers or other intestinal diseases.
- Patients with history of impairment of amino acid absorption.
- Patients with amino acid metabolic disorders including phenylketonuria
- Use with caution in patients with renal impairment

4.4 Special warnings and precautions for use

Whilst taking Uptamin Capsules both protein and energy are also required to provide complete nutrition in the daily diet. No other vitamins, minerals or supplements with or without vitamin A should be taken with this preparation except under medical supervision.

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

An allowance should be made for vitamins or minerals obtained from other sources.

4.5 Interaction with other medicinal products and other forms of interaction

VITAMIN B_6 (PYRIDOXINE)

Pyridoxine antagonizes the therapeutic action of levodopa by facilitating the transformation of levodopa into dopamine before levodopa can cross the blood-brain-barrier and enter the CNS.

VITAMIN B_{12} (CYANOCOBALAMIN)

Neomycin may impair absorption of vitamin B_{12}.

FOLIC ACID

- Phenytoin and possibly other related anticonvulsants may inhibit folic acid absorption.
- Folic acid supplementation may decrease serum phenytoin levels and complicate seizure control.
- Trimethoprim may act as a weak folic acid antagonist in humans.
- Pyrimethamine may induce megaloblastic anaemia in large doses.
- Metothrexate is a folic acid antagonist.

VITAMIN C

- Administration of vitamin concurrently with sulphonamides hinders solubility of sulphonamides increasing the risk of crystalluria.
- Acidification of the urine by vitamin C causes reabsorption of acidic drugs from the tubules, resulting in higher, more prolonged levels.
- The effect of basic drugs such as amphetamines and tricyclic antidepressants may be reduced by vitamin C.
- Vitamin C may increase the serum levels of oestrogens and reduce the anticoagulant effect of warfarin.

VITAMIN A

- Cholestyramine and mineral oil reduce the absorption of vitamins A,D and E. Avoid prolonged use.
- Large doses of vitamin A may increase the hypoprothrombic effect of warfarin.
- Oral contraceptive use may increase plasma levels of vitamin A.

VITAMIN D

- Phosphates from phosphate-containing drugs or magnesium-containing antacids may lower calcium levels and contribute to vitamin D deficiency.
- Phenytoin or barbiturates may decrease the half-life of vitamin D

VITAMIN E

- Enhancement of warfarin anticoagulation has been reported with long-term, high dose therapy of vitamin E.
- Iron hinders absorption of vitamin E.

4.6 Pregnancy and lactation

The normal rule that drugs should be avoided in the first trimester should be borne in mind.
Vitamin A doses above the Recommended Daily Allowance carries teratogenic risks.
Uptamin Capsules may be administered during pregnancy and lactation at the recommendation of the physician.

4.7 Effects on ability to drive and use machines

None anticipated.

4.8 Undesirable effects

Undesirable effects are listed by MedDRA System Organ Classes.

Assessment of undesirable effects is based on the following frequency groupings:

Very common: ≥1/10

Common: ≥1/100 to <1/10

Uncommon: ≥1/1,000 to <1/100

Rare: ≥1/10,000 to <1/1,000

Very rare: <1/10,000

Not known: cannot be estimated from the available data

Immune system disorders	*Not known:* Hypersensitivity reaction (such as rash)
Gastrointestinal disorders	*Not known:* Gastrointestinal disturbances (such as nausea, vomiting and abdominal pain)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions.

4.9 Overdose

No cases of overdosage due to Uptamin therapy have been reported. Any symptoms which may be observed due to the ingestion of large quantities of Uptamin capsules will be due to the fat soluble vitamin content. In the case of over dosage, which is very rare, the presenting symptoms are treated symptomatically after gastric lavage or evacuation has been done.

5. Pharmacological properties

5.1 Pharmacodynamic properties

The following account summarises the pharmacological effects of the vitamins and minerals in Uptamin Capsules and describes the conditions caused by deficiency of these.

L-LEUCINE

L- Leucine is a branched-chain amino acid that is an essential constituent of the diet and is not synthesized by the human body. It is the natural form of leucine. It is used as a dietary supplement. It is also an ingredient of several preparations that have been promoted for disorders of the liver.

L-ISOLEUCINE
L- Leucine is a branched-chain amino acid that is an essential constituent of the diet and is not synthesized by the human body. It is the natural form of leucine. It is used as a dietary supplement. It is also an ingredient of several preparations that have been promoted for disorders of the liver.

L-LYSINE HYDROCHLORIDE
L-Lysine Hydrochloride is an aliphatic amino acid that is an essential constituent of the diet. It is used as a dietary supplement.

L-PHENYLALANINE
L-Phenyl Alanine is an aromatic amino acid which is an essential constituent of the diet. It is used as a dietary supplement.

L-THREONINE
L-Threonine is a branched-chain amino acid which is an essential constituent of the diet. It is used as a dietary supplement. It has been investigated fro the treatment of various spastic disorders.

L-METHIONINE
L-Methionine is an essential amino acid and is therefore included in amino-acid solutions for parenteral nutrition.
Methionine also enhances the synthesis of glutathione and is used as an alternative to acetylcysteine in the treatment of paracetamol poisoning to prevent hepatotoxicity.
Methionine has been given orally to lower urinary pH and as an adjunct in the treatment of liver disorders.

L-TRYPTOPHAN
L-Tryptophan is an amino acid which is an essential constituent of the diet. It has been used as a dietary supplement.
Tryptophan is a precursor of serotonin. Because CNS depletion of serotonin is considered involved in depression, tryptophan has been used in its treatment.
It has generally been used as adjunctive therapy in depression. Pyridoxine and ascorbic acid are involved in the metabolism of tryptophan to serotonin and have sometimes been given concomitantly.

L-VALINE
L-Valine is an aliphatic amino acid which is an essential constituent of the diet. It is used as a dietary supplement. It is also an ingredient of several preparations that have been promoted for disorders of the liver.

VITAMIN B_1 (THIAMINE)
Thiamine is practically devoid of pharmacodynamic actions when given in usual therapeutic doses; even large doses produce no discernible effects. Isolated clinical reports of toxic reaction to the long-term parenteral administration of Thiamine probably represent rare instances of hypersensitivity.

The only established therapeutic use of Thiamine is in the treatment or the prophylaxis of Thiamine deficiency. The syndromes of Thiamine deficiency seen clinically can range from beriberi through wernicke's encephalopathy and korsakoff's syndrome to alcoholic polyneuropathy. Thiamine, a water-soluble vitamin, is an essential coenzyme for carbohydrate metabolism. Thiamine deficiency develops when the dietary intake is inadequate; severe deficiency leads to chronic beriberi characterized by peripheral neuritis, bradycardia, muscle weakness and paralysis.

VITAMIN B_2 (RIBOFLAVIN)

Riboflavine, a water-soluble vitamin, is essential for the utilization of energy from food. The active, phosphorylated forms, flavine mononucleotide and flavine adenine dinucleotide are involved as coenzymes in oxidative/reductive metabolic reactions.

Riboflavine deficiency develops when the dietary intake is inadequate. Deficiency leads to the development of a well-defined syndrome known as ariboflavinosis, characterized by cheilosis, angular stomatitis, glossitis and seborrhoeic keratosis of the nose and ano-genital region. There may be ocular symptoms including itching and burning of the eyes, photophobia and corneal vascularisation. Riboflavine deficiency may occur in association with other vitamin B complex deficiency states such as pellagra.

Riboflavine is used in the treatment and prevention of Riboflavine deficiency.

VITAMIN B_6 (PYRIDOXINE)

Pyridoxine, a water–soluble vitamin is involved principally in amino acid metabolism, but is also involved in carbohydrate and fat metabolism. It is also required for the formation of haemoglobin.

Deficiency of Pyridoxine is rare in humans due to its wide spread distribution in foods. Pyridoxine deficiency may however be drug induced and can occur, for instance, during isoniazid therapy. Inadequate Pyridoxine deficiency in adults lead to the development of peripheral neuritis, deficiency in children also affect the CNS.

Pyridoxine is used in the treatment and prevention of Pyridoxine deficiency states. Pyridoxine has also been used to treat seizure due to hereditary syndromes of Pyridoxine deficiency or dependency in infants. Pyridoxine has also been tried in a wide variety of other disorders, including the treatment of depression and other symptoms associated with the premenstrual syndrome and the use of oral contraceptives.

NICOTINAMIDE

Nicotinic acid and nicotinamide, the form that occurs naturally in the body are water-soluble vitamin B substances, which are converted to Nicotinanide Adenine Dinucleotide Phosphate (NADP). These coenzymes are involved in electron transfer reactions in the respiratory chain.

Nicotinamide deficiency develops when dietary intake is inadequate. Deficiency leads to the development of a syndrome known as pellagra characterized by skin lesions, especially on areas exposed to sunlight, with hyperpigmentation and hyperkeratinisation. Other symptoms include diarrhoea, abdominal pain, glossitis, stomatitis, and loss of appetite, headache, lethargy and mental and neurological disturbances. Nicotinic acid deficiency may occur in association with other vitamin B complex deficiency states.

Nicotinamide is used in the treatment and prevention of Nicotinic acid deficiency. Nicotinamide is preferred, as it does not cause vasodilatation.

CALCIUM D-PANTOTHENATE

Pantothenic acid is traditionally considered to be a vitamin B substance. It is a component of co-enzyme A which is essential in the metabolism of carbohydrate, fat and protein.

Deficiency of pantothenic acid is unlikely in man because of its wide spread distribution in food. It is administered as a nutritional supplement often as calcium salt and usually in conjunction with other vitamins of the B group.

Calcium regulates transport of other nutrients into the plant and is also involved in the activation of certain plant enzymes. Calcium deficiency results in stunting.

VITAMIN B_{12} (CYANOCOBALAMIN)

Vitamin B_{12}, water-soluble vitamins occur in the body mainly as methylcobalamin and as adenosylcobalamin and hydroxycobalamin. It act as coenzyme in nucleic acid synthesis.

Vitamin B_{12} deficiency may occur in strict vegetarians with an inadequate dietary intake, in patients with malabsorption syndromes or metabolic disorder, nitrous oxide induced megaloblastosis or following anaemias and neurological damage.

Vitamin B_{12} preparations are used in the treatment and prevention of Vitamin B_{12} deficiency. It is desirable to identify the cause of deficiency before commencing therapy. Treatment usually results in rapid haematological improvement and a striking clinical response.

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 DNA. It is also involved in some amino-acid conversions, and in the formation and utilisation of folates. Deficiency, which can result in megaloblastic anaemia, develops when the dietary intake is inadequate, as in malnutrition, from malabsorption, from increased utilization as in pregnancy or condition such as haemolytic anaemia.

Folic acid is used in the treatment and prevention of the folate deficiency state. It does not correct folate deficieny due to dihydrofolate reductase inhibition; Calcium folinate is used for this purpose.

VITAMIN C (ASCORBIC ACID)

Ascorbic acid, a water-soluble vitamin is essential for the synthesis of collagen and intercellular material. Ascorbic acid deficiency develops when the dietary intake is inadequate. Deficiency leads to the development of a well-defined syndrome known as scurvy characterized by capillary fragility, bleeding (especially from small blood vessel and the gum) anaemia, cartilage and bone lesions and slow healing of wounds.

Ascorbic acid is used in the treatment and prevention of Ascorbic acid deficiency. It completely reverses symptoms of deficiency. Ascorbic acid has been used to acidify urine and has also been tried in the treatment of idiopathic methaemoglobinaemia and many other disorders.

VITAMIN A

Vitamin A, a fat-soluble vitamin, is essential for growth, for the development and maintenance of epithelial tissue, and for vision, particularly in dim light. Vitamin A deficiency develops when the dietary intake is inadequate. Prolonged deficiency leads to xeropthalmia or 'dry eye' the initial symptoms of which is night blindness, which may progress to severe eye lesion and blindness. Other symptoms include changes in the skin and mucous membranes.

Vitamin A has also been used alone to treat various skin disorders including acne and Psoriasis.

VITAMIN D (CHOLECALCIFROL)

Cholecalciferol is the naturally occurring form of Vitamin D. It is produced from 7-hydrochlolesterol, a sterol present in mammalian skin by ultraviolet irradiation.

Vitamin D compounds are fat-soluble sterols, sometimes considered to be hormones or hormone precursors, which are essential for the proper regulation of calcium and phosphate homeostasis and bone mineralisation.

Vitamin D deficiency develops when there is inadequate exposure to sunlight or lack of the vitamin in the diet. Deficiency takes a long time to develop due slow release of the vitamin from body stores. It may occur in infants who are breast fed without supplemental vitamin D or exposure to sunlight, in the elderly whose mobility and thus exposure to light may be impaired, and in persons with fat malabsorption syndromes; certain disease states such as renal failure may also affect the metabolism of vitamin D substances to metabolically active forms and thus result in deficiency. Deficiency results in osteomalacia in adults. In children, rickets develops.

Vitamin D is uded in the treatment of vitamin D deficiency states and hypocalcaemia in disorders such as hypoparathyroidism and secondary hyper parathyroidism.

ALPHA TOCOPHERYL ACETATE (VITAMIN E)

Vitamin E, a fat-soluble vitamin prevents the oxidation of polyunsaturated fatty acids. It reacts with free radicals, which are the cause of oxidative damage to cell membranes, without the formation of another free radical in the process.

Vitamin E deficiency is rare but develops when the dietary intake is inadequate. In children with cystic fibrosis or biliary atresia, malabsorption of fat may lead to a vitamin E deficiency, deficiency may also occur in children with abnormalities of lipid transport, as in abetalipoproteinaemia. Low vitamin E concentrations are also found in premature, very low birth-weight infants. In previously healthy adults, malabsorption and low intake of vitamin E must continue for a number of years before signs of deficiency appear. The major signs of deficiency are the development of myopathic and neurological disorders.
Vitamin E is used for the treatment and prevention of vitamin E deficiency. Vitamin E is also used as an antioxidant in pharmaceutical manufacturing.

5.2 Pharmacokinetic properties
The following account describes the absorption and fate of each of the active constituents of Uptamin Capsules.

L-LEUCINE, L-ISOLEUCINE, L-LYSINE HYDROCHLORIDE, L PHENYLALANINE, L-THREONINE, L-VALINE
These amino acids are readily absorbed from the gastrointestinal tract. Excess amino acids are discarded, typically in the urine.

L-METHIONINE
About 80% of L-methionine ingested is converted to inorganic sulphate which is excreted in the urine. In the biosynthesis of cysteine, methionine is converted by demethylation to homocysteine which by enzymic condensation with serine forms cystathionine. In patients with homocystinuria the condensation process cannot proceed and homocysteine is converted to homocystine which is excreted in the urine.

L-TRYPTOPHAN
Tryptophan is readily absorbed from the gastrointestinal tract. It is extensively bound to plasma albumin. It is metabolized in the liver by tryptophan pyrrolase and tryptophan hydroxylase. Metabolites include hydroxytryptophan, which is then converted to serotonin and kynurenine derivatives. Some tryptophan is converted to nicotinic acid and nicotinamide. Pyridoxine and ascorbic acid are cofactors in the decarboxylation and hydroxylation, respectively of tryptophan; pyridoxine apparently prevents the accumulation of the kynurenine metabolites.

VITAMIN B_1 (THIAMINE)
Thiamine is well absorbed from the gastro intestinal tract following oral administration, although the absorption of large doses is limited. It is also rapidly absorbed following intra muscular administration. It is widely distributed to most body tissues and appears in breast milk. Thiamine is not stored to any appreciable extent in the body and amounts in excess of the body's requirements are excreted in the urine as unchanged Thiamine or as metabolites.
Thiamine requirements are directly related to the carbohydrate intake and the metabolic rate. A daily dietary intake of 1 to 1.3mg of Thiamine is recommended for healthy men and 0.7 to 1mg for healthy women.

VITAMIN B_2 (RIBOFLAVIN)
Riboflavine is readily absorbed from the gastro intestinal tract. Although Riboflavine is widely distributed to body tissues, little is stored in the body. Riboflavine is converted in the body to the coenzyme Flavine mononucleotide and then to another coenzyme Flavine adenine dinucleotide. About 60% of FMN and FAD are bound to plasma proteins. Riboflavine is excreted in urine, mainly as metabolites. As the dose increases, larger amounts are excreted unchanged. Riboflavine crosses the placenta and is distributed in breast milk.
The Riboflavine requirement is often related to the energy intake but it appears to be more closely related to the resting metabolic requirements. A daily dietary intake of about 1.3 to 1.8mg of Riboflavine is recommended.

VITAMIN B_6 (PYRIDOXINE)
Pyridoxine is readily absorbed from the gastro-intestinal tract following oral administration and is converted to the active forms pyridoxal phosphate and pyridoxamine phosphate. They are stored mainly in the liver where there is oxidation to 4-pyridoxic acid, which is excreted in the urine. Pyridoxine crosses the placenta and also appears in the breast milk.
For adults, the daily requirement of Pyridoxine is probably about 2mg and this amount is present in most normal diets. Meats, especially liver, cereals, eggs, fish and certain vegetables and fruits are good source of Pyridoxine.

NICOTINAMIDE
Nicotinamide is absorbed readily from all portions of the intestinal tract and the vitamin is distributed to all tissues. The principal route of metabolism of Nicotinic acid and nicotinamide is by the formation of N—methylnicotinamide, which in turn is metabolized further. Small amounts of the unchanged vitamins appear in the urine following therapeutic doses of nicotinic acid and nicotinamide.
The daily adult requirement is probably about 15-20mg.

CALCIUM PANTHOTHENATE
Pantothenic acid is readily absorbed from the gastro intestinal tract following oral administration. It is widely distributed in the body tissues and appears in breast milk. About 70% of Pantothenic acid is excreted unchanged in the urine and about 30% in the fences.
Pantothenic acid is rapidly absorbed in foods-meat, legumes and whole grain cereals are particularly rich sources. Recommended daily intakes of Pantothenic acid have not been set, but human requirements are adequately met by a daily intake of about 4 to 10mg.

VITAMIN B_{12} (CYANOCOBALAMIN)
Vitamin B_{12} substances bind to intrinsic factor and are then actively absorbed from the gastro intestinal 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.
Vitamin B_{12} is extensively bound to specific plasma proteins called Transcobalamins, Transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. It is stored in the liver, excreted in the bile and undergoes enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours. Vitamin B_{12} diffuses across the placenta and also appears in breast milk.
For adults, the daily requirement of Vitamin B_{12} is probably about 1 to 3µg and this amount is present in most normal diets.

FOLIC ACID
Folic Acid is absorbed mainly from the small intestinal. The naturally occuring folate polyglutamates are largely deconjugated and reduced prior to absortion. It is the 5-methyterahydrofolate, which appears in the portal circulation, where it is extensively bound to plasma proteins.
Folic acid is rapidly absorbed from normal diets and is distributed in body tissues. The principal storage site is the liver. There is an enthroheptic circulation for folate, about 4 to 5η is excreted in the urine daily. Administration of larger doses of folic acid leads to proportionately more of the vitamin being excreted in the urine. Folate is distributed into breast milk.
Body-store folate in healthy persons have been reported as being between 5 to 10mg, but may be much higher, About 400mg of folate a day is considered a suitable average intake. Folate is present, chiefly combined with several L (+) – glutamic acid moieties in many foods. The vitamin is readily oxidized to unavailable forms and is easily destroyed during cooking.

VITAMIN C (ASCORBIC ACID)
Ascorbic acid is readily absorbed from the gastro intestinal tract and is widely distributed in the body tissues. It is reported to be 25% bound to plasma proteins. The amount of ascorbic acid in the body in health is about 1.5g. The concentration is higher in leucocytes and platelets than in erythrocytes and plasma. In deficiency states the concentration in leucocytes declines later and at a slower rate, and has been considered to be a better criterion for the evaluation of deficiency than the concentration in plasma.

Ascorbic acid is reversibly oxidised to dehydroascorbic acid; some is metabolised to ascorbate – 2 – sulphate, which is inactive and oxalic acid, which are excreted in the urine. Ascorbic acid in excess of the body's needs is also rapidly eliminated in the urine. Ascorbic acid crosses the placenta and is distributed into breast milk. It is removed by haemodialysis.
A daily dietary intake of about 30 to 60mg Ascorbic acid has been recommended for adults. There is, however, wide variation in individual requirements. Humans are unable to form their own ascorbic acid and so a dietary source is necessary. Most dietary ascorbic acid is obtained from fruit and vegetable sources; only small amounts are present in milk and animal tissues.

VITAMIN A
Vitamin A is readily absorbed from the gastro intestinal tract but absorption may be reduced in the presence of fat malabsorption, low protein intake, or impaired liver or pancreatic function. Vitamin A esters are hydrolyzed by pancreatic enzymes to retinol, which is then absorbed. Some retinol are stored in the liver.
It is released from the liver bound to a specific α_1 – globulin (retinol – binding protein) in the blood. The retinol not stored in the liver undergoes glucuronide conjugation and subsequent oxidation to retinal and retinoic acid, these and other metabolites are excreted in urine and faeces. Vitamin A does not readily diffuse across the placenta but is present in the milk of nursing mothers.

VITAMIN D (CHOLECALCIFROL)
Vitamin D substances are well absorbed from the gastrointestinal tract. The presence of bile is essential for adequate intestinal absorption; absorption may be decreased in patients with decreased fat absorption.
Vitamin D and its metabolites circulate in the blood bound to a specific α-globulin. Vitamin D can be stored in adipose and muscle tissues for long periods of time. It is slowly released from such storage sites and from the skin where it is formed in the presence of sunlight or ultraviolet light. Ergocalciferol and cholecalciferol have a slow onset and a long duration of action.
Cholecalciferol and ergocalciferol are hydroxylated in the liver by the enzyme vitamin D 25-hydroxylase to form 25-hydroxycholecalciferol (calcifediol) and 25- hydroxyergocalciferol respectively. These compounds undergo further hydroxylation in the kidneys, including the formation of the 1,24,25-trihydroxy derivatives. Of the synthetic analogues, alfacalcidol is converted rapidly in the liver to calcitriol, and dihydrotachysterol is hydroxylated, also in the liver, to its active form 25-hydroxydihydrotachysterol.
Vitamin D compounds and their metabolites are excreted mainly in the bile and faeces with only small amounts appearing in the urine; there is some enterohepatic recycling but it is considered to have a negligible contribution to vitamin D status. Certain vitamin D substances may be distributed into breast milk.

ALPHA TOCOPHERYL ACETATE (VITAMIN E)
Absorption of vitamin E from the gastrointestinal tract is dependent on the presence of bile and on normal pancreatic function. The amount of vitamin E absorbed varies widely between about 20% and 80% and appears to decrease as the dose is increased. It enters the blood via the chylomicrons in the lymph and is bound to beta lipoproteins. It is widely distributed to all tissues, and stored in adipose tissue. Some vitamin E is metabolized in the liver to glucuronides of tocopheronic acid ant its ٢-lactone. Some is excreted in the urine, but most of a dose is slowly excreted in the bile. Vitamin E appears in breast milk but is poorly transferred across the placenta.

5.3 Preclinical safety data
There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6. Pharmaceutical particulars

6.1 List of excipients
Aminoacid and multivitamin pellets.

6.2 Incompatibilities
No major incompatibilities are known.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Store below 30°C.

Protect from light.

6.5 Nature and contents of container
The product is presented in blister strip is composed of PVC/ with a printed aluminium foil.

The product is available in packs of 20 capsules.

6.6 Special precautions for disposal and other handling
Not applicable.

7. Applicant/Manufacturer
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