National Agency for Food & Drug Administration &

Control (NAFDAC)

Registration & Regulatory Affairs (R & R) Directorate

SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

1. NAME OF THE MEDICINAL PRODUCT

Astymin SN (Pure crystalline Aminoacids intravenous infusion with xylitol)

Strength

Each ml contains

L-Isoleucine	USP	5.6mg
L-Leucine	USP	12.5mg
L-Lysine Hydrochloride	USP	11.0mg
L-Methionine	USP	3.5mg
L-Phenylalanine	USP	9.35mg
L-Threonine	USP	6.5mg
L-Tryptophan	USP	1.3mg
L-Valine	USP	4.5mg
L-Alanine	USP	6.2mg
L-Arginine hydrochloride	USP	9.55mg
L-Aspartic acid	BP	3.8mg
L-Cysteine hydrochloride	USP	1.45mg
L-Glutamic acid	BP	6.5mg
L-Histidine hydrochloride H2O	BP	8.11mg
L-Proline	USP	3.3mg
L-Serine	USP	2.2mg
L-Tyrosine	USP	0.35mg
Glycine	USP	10.7mg
Xylitol	USP	50.0mg

Pharmaceutical dosage form: Intravenous Infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Batch size: 1000 Litres

Ingredients	Specification	Label Claim (mg)	Overage	Quantity added (mg) /ml	Quantity added (kg) /batch
L-Isoleucine USP	USP	5.600	---	5.600	5.600
L-Leucine	USP	12.500	---	12.500	12.500
L-Lysine Hydrochloride USP	USP	11.000	---	11.000	11.000
L-Methionine	USP	3.5000	---	3.5000	3.5000
L-Phenylalanine	USP	9.3500	---	9.3500	9.350
L-Threonine	USP	6.500	---	6.500	6.500
L-Tryptophan	USP	1.300	4%	1.350	1.350
L-Valine	USP	4.500	---	4.500	4.500
L-Alanine	USP	6.200	---	6.200	6.200
L-Arginine hydrochloride	USP	9.550	---	9.550	9.550
L-Aspartic acid	BP	3.800	---	3.800	3.800
L-Cysteine hydrochloride	USP	1.450	---	1.450	1.450
L-Glutamic acid	BP	6.500	---	6.500	6.500
L-Histidine hydrochloride H_2O	BP	8.110	---	8.110	8.110
L-Proline	USP	3.300	---	3.300	3.300
L-Serine	USP	2.200	---	2.200	2.200
L-Tyrosine	USP	0.350	3%	0.360	0.360
Glycine	USP	10.700	---	10.700	10.700
Xylitol	USP	50.000	---	50.000	50.000
Water for injections	BP	q.s.	---	q.s.	q.s.

USP : United States Pharmacopoeia
BP : British Pharmacopoeia

3. PHARMACEUTICAL FORM

A colourless clear solution.

4. Clinical particulars

4.1 Therapeutic indications

Internal Medicine	Surgery
Persistent Prexial States	Pre & Post-operative conditions
Severe malnutrition	Burns
Malignant disease	Accidental trauma
Malabsorption in G.I disorder	Fracture of long bones

4.2 Posology and method of administration

Adult: 200 - 800 ml intravenously per day.

Children: 0.2 – 0.25 gm of nitrogen/kg body weight

Drip rate: 15 - 20 drops initially followed by 30 – 40 drops per minute.

Method of administration: Intravenous infusion

4.3 Contraindications

Hypersensitivity to amino acids, cardiac insufficiency, irreversible liver damage.

4.4 Special warnings and precautions for use

Not to be used if any suspended matter is present.

Astymin-SN IV Infusion should be used with caution in patient with diabetes mellitus, severe heart failure or with renal function in combination with fluid restriction or oliguria/anuria of other origin. In patients with hyperglycemia, administration of exogenous insulin might be necessary. Feeding of carbohydrates in severely malnourished patients can trigger a thiamine (Vitamin B1) deficiency syndrome.

The drip rate initially should be 15 to 20 drops per minute, followed by 30 to 40 drops per minute. Signs of intolerance and increased renal losses resulting in amino acids disequilibrium possible infusion rate is too rapid.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction between Astymin SN and medications occur in three main ways; physiological interactions that occur at all times, altered behaviour of medications owing to the complications of the presenting condition or sub.optimal nutritional support and direct chemical interaction in the tubing during administration. Mixing of medications with PN in administration lines should be avoided unless validated by the manufacturer or accredited laboratory. Medications known to affect plasma protein binding of bilirubin should be avoided in parenterally fed newborn patients with severe hyperbilirubinaemia.

Astymin-SN Infusion should not be administered along with Mannitol. Mannitol being an osmotic diuretic, the infused will be rapidly excreted from the body.

4.6 Pregnancy and Lactation

Animal reproduction studies have not been conducted with Astymin-SN-Infusion. It is not known whether Astymin-SN-Infusion, (a crystalline amino acid with xylitol solution) can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Astymin-3 infusion should be given to a pregnant woman only if clearly needed.

4.7 Effects on ability to drive and use machines

Not Known

4.8 Undesirable effects

Local reactions consisting of, erythema, phlebitis and thrombosis at the infusion site have occurred with peripheral intravenous infusion of amino acids particularly if other substances, such as antibiotics, are also administered through the same site. In such cases the infusion site should be changed promptly to another vein. Use of large peripheral veins, inline filters and slowing the rate of infusion may reduce the incidence of local venous irritation. Electrolyte additives should be spread throughout the day. Irritating additive medication may need to be injected at another venous site.

Generalized flushing, fever and nausea also have been reported during peripheral infusion of amino acids solutions.

4.9 Overdose

If Astymin-SN IV Infusion is administered at a higher rate than recommended, there is an augmented risk for nausea, vomiting and sweating. When peripheral veins are used thrombophlebitis may occur. Osmotic diuresis with dehydration may occur if the dosage recommendations are exceeded. There is also a risk of symptoms related to hyperglycemia with Astymin-SN IV Infusion. In case of symptoms due to overdose, the infusion should be slowed down or discontinued.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Preserving glutathione levels; Protecting the nitric oxide (NO) cycle; and Reacting with and inactivating inflammatory mediators such as cytokines and prostaglandins.

Astymin-SN Injection contains pure Crystalline amino acids with Xylitol. Protein hydrolysis, in which protein have been reduced to short -chain peptides and amino acids, long have been used orally or relatively dilute solutions intravenously as supplementary nutrients for patients unable to metabolize intake protein adequately. For patients in whom oral or tube feeding is contra-indicated or inadequate good nutrients may achieve and maintained, for several months if necessary, by the procedure intravenous feeding known as total parenteral (TPN) nutrients.

The most critical component in TPN is a nitrogen source available for repletion and /or maintenance of lean body mass and proteins essential for wound healing, tissue repair and growth. The physiological availability of these amino acids are outlined here under.

Astymin-SN provides a physiological ratio of biologically utilizable essential and non-essential amino acids with xylitol to meet adult requirements. The amino acids provide a substrate for protein synthesis as well as sparing body protein and muscle mass. Peripheral intravenous infusion of amino acids administered for short periods in selected patients promote protein anabolism and prevent protein breakdown to meet caloric requirements.

5.2 Pharmacokinetic properties

Crystalline L-Amino acids appear to be more efficiently metabolized and better tolerated in the body.

Amino acids after entering the blood are rapidly removed from there to the liver, while others pass into the systemic circulation and reach the tissues where they replace the corresponding amino acids of the protoplasmic proteins. The amino acids form a pool that supplies the needs of the body. In the kidney most of the filtered amino acids are reabsorbed.

The amino acid pool represents the stores available for protein synthesis. The amino acids of the body pool are derived from proteins in the diet and constant breakdown of tissue proteins. All amino acids under go one or other of the following changes:

Conversion into another amino acid through a metabolic cycle. For example, (a) glycine can form serine and N-free precursors; (b) arginine can be synthesized from CO_2 and NH_3 derived from the metabolism of amino acids; (c) by direct transamination where an amino group of one amino acid is shifted to a keto acid in the presence of the enzyme transaminase as α-ketoglutaric acid an alanine giving pyruvic acid and glutamic acid.

When all the necessary amino acids are present, they may be condensed into protein. This is shown by the finding that an essential amino acid tagged with radioactive carbon is converted into protein only if all the constituent amino acids for the required protein are simultaneously present. Otherwise, the amino acid is degraded and excreted within a few hours. As long as the protein intake is mixed, there is a pool of amino acids for the synthesis of proteins. This is of practical importance. A mixture of protein containing foods taken at one meal is better utilized for tissue growth than a single protein rich food which may not contain all the required amino acids.

Amino acids may be delaminated to form α-ketoacids and ammonia. α-ketoacids may be oxidized further to yield energy or are utilized for synthesis of carbohydrates and fats.

During growth, the equilibrium between amino acids and body proteins shift towards the latter so that synthesis exceeds breakdown. At all ages, a small amount of protein is lost as hair. Some small proteins are lost in the urine, and there are un-reabsorbed protein digestive secretions in the stool. These losses are made up by synthesis from the amino acid pool.

Thyroxine, catecholeamines, histamines, serotonins, melatonin and intermediates in the urea cycle are formed from specific amino acids. Methionine, cysteine, and cystine provide the sulphur contained in proteins, for enzyme A, taurine and other biologically important compounds. Methionine is converted into S-adenosyl methonine, which is the active methylating agent in the synthesis of compounds such as ephinephrine, acetylcholine, and creatine. It is a major donor of biological labile methyl groups, but methyl groups can also be synthesized from a derivative of formic acid bound to folic acid derivatives if the diet contains adequate amounts of folic acid and cynocobalamin.

Oxidative deamination of amino acids occurs in the liver. An imino acid is formed by dehydrogenation and this compound is hydrolyzed to the corresponding keto acid with the liberation of ammonia. Amino acids can also take up NH3 forming the corresponding amide. An example is the binding of NH3 in the brain by glutamic acid. The reverse reaction occurs in the kidney with the liberation of NH3 into the urine. The NH3 reacts with the H+ to form NH4 + thus permitting more H+ to be secreted into the urine. Most of the NH3 formed by deamination of amino acids in the liver is converted to urea, and the urea is excreted in the urine. Except for the brain, the liver is probably the only site of urea formation.

Normally the rate of supply of amino acids approximately equals the needs of tissues for growth and repair. Limited amounts of amino acids are stored in the body in a pool which is largely intracellular.

Average normal excretion of amino acids is about 150mg of free acids or between 400mg and 1gm of total acid in 24hours. Most of the NH3 formed by deamination of amino acids in the liver is converted to urea, and the urea is excreted in the urine. Except for the brain, the liver is probably the only site of urea formation.

5.3 Preclinical safety data

Not known

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

S.No	Ingredients	Specification
1.	Water for injections	BP

6.2 Incompatibilities: Not Applicable

6.3 Shelf life: 24 months from the data of manufacturing

6.4 Special precautions for storage: Store below 30°C. Protect from light.

6.5 Nature and contents of container:

Bottles are of USP Type II (200ml). Packed in an individual carton.

6.6 Special precautions for disposal: Not Applicable

7. APPLICANT / MANUFACTURER:

APPLICANT:

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