Australian Product Information – Vamin® 14, Vamin® 14 Electrolyte Free, Vamin® 18 Electrolyte Free (amino acids) solution for infusion

1 NAME OF THE MEDICINE

Vamin 14 – Alanine, arginine, aspartic acid, cysteine hydrochloride monohydrate, glutamic acid, glycine, histidine, isoleucine, leucine, lysine hydrochloride, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, calcium gluconate monohydrate, magnesium sulfate heptahydrate, potassium chloride, sodium acetate trihydrate.

Vamin 14 Electrolyte Free & Vamin 18 Electrolyte Free – Alanine, arginine, aspartic acid, cysteine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine acetate, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Clear, colourless to slightly yellow solution.

Table 1.	Vamin 14		Vamin 14 Electrolyte Free		Vamin 18 Electrolyte Free	
	g/L	% of total amino acids	g/L	% of total amino acids	g/L	% of total amino acids
Isoleucine	4.2	4.92	4.2	4.92	5.6	4.92
Leucine	5.9	6.92	5.9	6.92	7.9	6.94
Valine	5.5	6.45	5.5	6.45	7.3	6.41
Phenylalanine	5.9	6.92	5.9	6.92	7.9	6.94
Methionine	4.2	4.92	4.2	4.92	5.6	4.92
Lysine	6.8[1]	7.97	6.8[2]	7.97	9.0[2]	7.90
Threonine	4.2	4.92	4.2	4.92	5.6	4.92
Tryptophan	1.4	1.64	1.4	1.64	1.9	1.67
Cysteine	0.42[3]	0.49	0.42	0.49	0.56	0.49
Histidine	5.1	5.98	5.1	5.98	6.8	5.97
Tyrosine	0.17	0.20	0.17	0.20	0.23	0.17
Alanine	12.0	14.06	12.0	14.06	16.0	14.05
Arginine	8.4	9.85	8.4	9.85	11.3	9.92
Aspartic acid	2.5	2.93	2.5	2.93	3.4	2.99
Glutamic acid	4.2	4.92	4.2	4.92	5.6	4.92
Glycine	5.9	6.92	5.9	6.92	7.9	6.94
Proline	5.1	5.98	5.1	5.98	6.8	6.97
Serine	3.4	3.99	3.4	3.99	4.5	3.95
Total Nitrogen	13.5		13.5		18.0	
Amino acid concentration (% by weight)		8.5		8.5		11.4

1 as hydrochloride
2 as acetate
3 as hydrochloride monohydrate

Table 2.	Vamin 14	Vamin 14 Electrolyte Free	Vamin 18 Electrolyte Free
Calcium Gluconate H_2O	2.24 g/L		
Potassium chloride	3.73 g/L		
Sodium acetate $3H_2O$	13.6 g/L		
Magnesium sulfate $7H_2O$	1.97 g/L		
Osmolality mOsm/kg H_2O	1145	810	1130
pH	5.4 – 5.8	5.4 – 5.8	5.4 – 5.8
Na^+ (mmol/1000 mL)	100		
K^+ (mmol/1000 mL)	50		
Ca^{++} (mmol/1000 mL)	5		
Mg^{++} (mmol/1000 mL)	8		
Cl^- (mmol/1000 mL)	100		
Acetate (mmol/1000 mL)	135		
Sulfate (mmol/1000 mL)	8		

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Injection, intravenous infusion.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Vamin 14, Vamin 14 Electrolyte Free

Intravenous supply of amino acids to patients with moderately increased requirements who are unable to receive sufficient amounts of protein enterally.

Vamin 18 Electrolyte Free

Intravenous supply of amino acids specially to patients with highly increased requirement who are unable to receive sufficient amounts of protein enterally. Vamin 18 is also indicated where there is a need to control the total amount of fluid being given to a patient.

Vamin 18 has been shown to reduce nitrogen loss in patients with major burns without sepsis.

Vamin 14 and 18 should be administered by personnel experienced in intravenous nutrition.

4.2 Dose and method of administration

Dosage

Total daily dose of the solution should be adjusted to the individual patient's metabolic requirements for clinical response. The determination of nitrogen balance and accurate daily bodyweights corrected for fluid balance are probably the best means of assessing individual nitrogen requirements (see Section 4.4 Special warnings and precautions for use, Clinical monitoring). It is essential that a carefully prepared protocol based on current medical practices be carried out only by personnel experienced in parenteral nutrition.

Adults
Up to 1 litre intravenously per day depending upon calculated protein requirements. The infusion time of 1 litre of amino acid solution should be eight hours or more.

Reliable intravenous pump or drip controls are needed to obtain the desired control over the infusion rate. The protein requirement for Vamin 14 and Vamin 18 will need to be calculated in accordance with an appropriate schedule (see Section 4.4 Special warnings and precautions for use, Clinical monitoring) (Lee & Hartley, 1975).

Usual amino acid requirements are of the order of 1 to 2 g/kg/24 hours although the losses may increase in catabolic state to 3 g/kg/24 hours or more. It is not possible nor desirable to compensate large losses at the time but during recovery.

Use in the elderly
Dosage as for adults except when hepatic or renal insufficiency is present.

Accepted values for the amount of energy required per g nitrogen are 150 to 200 Kcal/g (150:1 to 200:1 Kcal/g N) for normally metabolising man and 163:1 Kcal/g N for post-operative non-septic patients. Patients with major burns are hypermetabolic and formulas in use recommend 20 Kcal/kg plus 70 Kcal per % burn for energy, and 1 g/kg plus 3 g per % burn for protein. Because of the need to control fluid input, concentrated amino acid solutions will be required in some of these patients.

Impaired liver function
Contraindicated in patients with severe liver diseases. Conservative doses should be given to patients with known or suspected hepatic dysfunction as serum amino acid imbalance, hyperammonaemia, stupor and coma may result. Should symptoms of hyperammonaemia develop, administration should be discontinued and the patient's clinical status re-evaluated.

Method of administration

Strongly hypertonic nutrient solutions are best administered by a catheter into the low superior vena cava or right atrium. Glucose-saline solutions should be used until radiological confirmation of the site of the catheter tip is obtained.

There are no data on the compatibility of Vamin 14 and 18 with other parenteral products.

4.3 Contraindications

In the case of Vamin 14 (with electrolytes): Severe liver damage

Hyperkalaemia: Severe renal disease or impaired renal function; parenteral nutrition should only be administered when fluid and electrolyte balance can be maintained.

The supply of amino acids can result in increased ureagenesis and methods should be available to cope with this, viz. dialysis.

4.4 Special warnings and precautions for use

Vamin 14 and 18 have low cysteine and tyrosine content and are not designed for paediatric use.

A turbid solution should not be infused. The contents of each bottle are for a single infusion only. Any remaining solution should be discarded.

Vamin 14 and 18 have not been tested in patients with hepatic failure, hepatic encephalopathy or multi system organ failure. In severe sepsis or other highly catabolic (greater than 150 g/day) states, these formulations may not be optimal.

Monitoring during administration

When Vamin 14 and 18 infusions are administered to patients, clinical and laboratory observations must be made regularly and routinely to ensure safety. Severely ill, metabolically unstable patients require close and special monitoring.

Caloric requirements

It is essential to provide for appropriate caloric supply concurrently if parenterally administered amino acids are to be retained by the body and utilised maximally for protein synthesis. Concentrated glucose solutions or fat emulsions are effective sources of such calories. In septic patients, fat and glucose utilisation are impaired, and glucose and Intralipid should be given as tolerated.

Clinical monitoring

A basic outline of monitoring requirements is given below; for full details see Transactions of Australian Society for Parenteral and Enteral Nutrition. (Vol. 1 P.32 September, 1984).

1 *Four hourly check*
   a) Patient – comfort, conscious state, change in overall condition, vital signs.
   b) Infusion apparatus and rate.

2 *Daily assessment*
   a) Balance chart – nitrogen (or protein equivalent); glucose (or other carbohydrate used as energy source); fat (as lipid emulsion); total non-protein energy; electrolytes; fluid.
   b) For calculation of daily nitrogen requirements see, e.g. Lee & Hartley. Postgrad. Med. J. 1975; 51: 441-5.
   c) Full blood examination if sepsis suspected.

3 *Alternative day assessment*
   a) Routine clinical chemistry screen (until patient clinically and metabolically stable then twice weekly.
   b) Full blood examination: prior to therapy and then 2-3 times weekly.

4 *Weekly assessment*
   Extra clinical chemistry to assess renal and hepatic function and bone mineral status.

5 *Specific assessments*
   Trace metals, vitamins, amino acids, coagulation studies, blood cultures, blood gases and 24-hour urine analysis should be carried out whenever clinically indicated.

Catheter management

A chest radiograph is mandatory after insertion of a central intravenous catheter to check positioning of the catheter tip and to exclude pneumothorax caused by the insertion technique.

Placement of central venous catheters

Strongly hypertonic nutrient solutions must be administered by a catheter inserted into the low superior vena cava. Insertion into the right atrium may be a controversial matter and only soft catheters must be used for this. Radiographic confirmation of the correct position of the tip of the central venous catheter must be obtained before the infusion of hypertonic nutrient solutions. Infusion of hypertonic solutions into a catheter misplaced up the internal jugular will lead to major thrombosis. Repeat X-rays are advisable every 14 days, unless there is any clinical suspicion of dislodgement, in which a chest X-ray is immediately indicated.

Complications arising from the techniques of administration

The most serious problems of central vein parenteral nutrition are related to the techniques of administration of the nutrition solution. Sepsis or septicaemia are the most important complications.

Prevention of infection requires specialised care of the central catheter, infusion line and nutrition bottle. Antibiotics may be necessary; however, catheter sepsis can only be cured by removal of the catheter.

Pneumothorax and haemothorax are complications which may occur during catheter placement. Large vein thrombosis is a possible complication of vena cava catheterisation. The insertion of a central venous catheter through the femoral vein should be avoided because of complications. Extravasation of nutrition solution may cause tissue damage and possibly necrosis. Other complications, e.g. arterial puncture and transection, injury to branchial plexus, formation of arteriovenous fistula, cardiac arrhythmia and catheter embolus can be avoided by careful technique.

Complications

Complications associated with rate of delivery

The common metabolic disorders associated with too rapid delivery of nutrition solutions are hyperglycaemia, glycosuria and aminoaciduria, leading to dehydration. Conversely, hypoglycaemia may occur if the solution is suddenly slowed or stopped. A constant delivery rate is essential to prevent these complications. Hyperammonaemia has been reported as a complication of parenteral nutrition.

Hypophosphataemia

Inadequate phosphate administration may cause haemolysis and neurological signs. When commencing intravenous nutrition 25 to 50 mmol/day may be required reducing to 10 to 25 mmol/day when the patient is established.

Hyperchloraemic metabolic acidosis

A reported complication of parenteral nutrition may occur with administration of Vamin solutions.

Fluid balance

Care should be taken to avoid hypervolaemia particularly in patients with cardiac insufficiency and pulmonary disorders. Hypertonic glucose solutions should not be used.

Vitamin supplementation

With long term hyperalimentation or in patients with overt or suspected deficiency attention should be paid to appropriate vitamin supplementation. See Transaction of Australian Society for Parenteral and Enteral Nutrition. 1984, 1, 23-24.

Deficiency of essential fatty acids has been shown to occur within 7 to 10 days of fat free total parenteral nutrition. It is, therefore, recommended that a fat emulsion preparation be used as a source of essential fatty acid for any patient who is on total parenteral nutrition by the central route for longer than 7 days.

Use in hepatic impairment

See Section 4.3 Contraindications.

Use in renal impairment

See Section 4.3 Contraindications.

Use in the elderly

No data available.

Paediatric use

Vamin 14 and 18 have low cysteine and tyrosine content and are not designed for paediatric use.

Effects on laboratory tests

No data available.

4.5 Interaction with other medicines and other forms of interaction

No data available.

4.6 Fertility, pregnancy and lactation

Effects on fertility

No data available.

Use in pregnancy

There have been successful pregnancies in patients on parenteral nutrition. However, safety of Vamin 14 and Vamin 18 in pregnancy has not been established.

Use in lactation

There is no information on the use of Vamin 14 and Vamin 18 in nursing mothers.

4.7 Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration.

4.8 Adverse effects (Undesirable effects)

Infusion that is too rapid may cause fever, chills, nausea and vomiting. Complications which may occur with administration for intravenous amino acid preparations are:

Allergic Reactions:	Hypersensitivity to one more amino acids.
Biochemical:	Increased serum AST and ALT; increased BUN and serum alkaline phosphatase; electrolyte imbalances particularly hypokalaemia and hypophosphataemia; hyperammonaemia; decreased serum osmolality; acid-base imbalances; hyperchloraemic metabolic acidosis.
Cardiovascular:	Disturbances of venous circulation; large vein thrombosis, catheter embolus, septicaemia, cardiac arrhythmias.
Gastrointestinal:	Nausea.
Injection site:	Catheter sepsis; localised inflammation; damage to vein walls, thrombophlebitis; extravasation of parenteral solution.
Respiratory:	Pneumothorax; haemothorax.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 Overdose

For information on the management of overdose, contact the Poisons Information Centre on 13 11 26 (Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

Vamin 14, Vamin 14 Electrolyte Free and Vamin 18 Electrolyte Free contain all 18 essential and non-essential amino acids but in different concentrations. One litre of Vamin 14 and Vamin 14 Electrolyte Free contains amino acids corresponding to nitrogen 13.5 g.

Vamin 18 Electrolyte Free is a more concentrated solution containing nitrogen 18 g. (For details see Section 2 Qualitative and Quantitative Composition).

Vamin 14 and 18 are appropriate for patients who have an increased protein turnover and hence requirement, but are utilising relatively normal metabolic pathways. The essential amino acid to total nitrogen ratio (E/T ratio) is 2.82 for both formulations.

Clinical trials

No data available.

5.2 Pharmacokinetic properties

Metabolism

Vamin amino acid solutions provide a source of 8 essential and 10 non-essential amino acids for metabolic processes involved in protein synthesis. Amino acids in excess of immediate requirements are either metabolised in alternative pathways, catabolized and/or excreted.

Initial distribution of most amino acids takes place via the central vascular compartment and extravascular water and transported into cells. Amino acids actively transported into cells where incorporation into proteins, conversion to other amino acids, degradation for fuel or deamination occurs.

For metabolism and requirements for individual amino acids please refer to standard biochemical texts.

Excretion

Amino acids are excreted in the renal tubules and an active transport mechanism is responsible for resorbing amino acids from the glomerular filtrate and returning them to the circulation. There is an upper limit to the capacity of this active transport system beyond which excess amino acids are excreted in the urine.

5.3 Preclinical safety data

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Glacial acetic acid
- Water for injections.

6.2 Incompatibilities

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 Shelf life

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

Glass bottle:
Vamin 14 – 500 mL (AUST R 14456), 1000 mL (AUST R 48240)
Vamin 14 Electrolyte Free – 500 mL (AUST R 144556), 1000 mL (AUST R 48235)
Vamin 18 Electrolyte Free – 500 mL (AUST R 14454), 1000 mL (AUST R 48237).

6.6 Special precautions for disposal

In Australia, any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 Physicochemical properties

The physicochemical properties of this medicine were not assessed as part of its registration.

7 MEDICINE SCHEDULE (POISONS STANDARD)

Not scheduled.

8 SPONSOR

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9 DATE OF FIRST APPROVAL

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10 DATE OF REVISION

15 November 2019

Summary Table of Changes

Section changed	Summary of new information
n.a.	reformatted PI