1. NAME OF THE MEDICINAL PRODUCT.

Amiparen® 10%

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 ml solution contains:

Ingredient	**100 mL**
L-Leucine	1.4g
L-Isoleucine	0.8 g
L-Valine	0.8 g
L-Lysine Acetate	1.48 g
(L-Lysine equivalent)	(1.05 g)
L-Threonine	0.57g
L-Tryptophan	0.2 g
L-Methionine	0.39 g
L-Cysteine	0.1 g
L-Phenylalanine	0.7 g
L-Tyrosine	0.05 g
L-Arginine	1.05 g
L-Histidine	0.5g
L-Alanine	0.8 g
L-Proline	0.5 g
L-Serine	0.3 g
Glycine	0.59g
L-Aspartic Acid	0.1g
L-Glutamic Acid	0.1g

3. PHARMACEUTICAL FORM

Amiparen® 10% is a clear and colorless or slightly yellow solution for intravenous infusion.
PH range: 6.5–7.5
Osmotic pressure ratio (relative to physiological saline): Approx. 3.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Provision of amino acids in the following instances: hypoproteinemia, malnutrition, and before and after surgery.

4.2. Posology and method of administration

1. Infusion via central vein

The usual adult dose of **Amiparen® 10%** is 400–800 mL per day, infused via a central vein. The dose should be adjusted according to the patient's age, symptoms, and body weight.

2. Infusion via peripheral vein

The usual adult dose of **Amiparen® 10%** is 200–400 mL per dose, infused via a peripheral vein. The infusion rate may be adjusted to provide about 10 g of amino acids over 60 minutes in order to achieve optimal utilization of amino acids. The standard infusion rate in adults is 100 mL over 60 minutes. The rate should be slowed in children, the elderly, and seriously ill patients. Dose should be adjusted according to patient's age, symptoms, and body weight.
A combination of **Amiparen® 10%** with a carbohydrate solution is highly recommended for more efficient utilization of amino acids.

4.3. Contraindications

Amiparen® 10% is contraindicated in the following patients.

(1) Patients with hepatic coma or a risk of hepatic coma [Because of inadequate amino acid metabolism, the patient's clinical condition may be worsened.]
(2) Patients with serious renal disorders or azotemia (for both, patients on dialysis or hemofiltration are exclude [Urea and other amino acid metabolites may be retained, which may worsen the patient's clinical condition.] (See section **Special warnings and precautions for use)**
(3) Patients with abnormal amino acid metabolism [Because the infused amino acids are not adequately metabolized, the patient's clinical condition may be worsened.]

4.4. Special warnings and precautions for use

1. Careful Administration (Amiparen® 10% should be administered with care in the following patients.)
(1) Patients with severe acidosis [The patient's clinical condition may be worsened.]
(2) Patients with congestive cardiac failure [An increase in the circulating blood volume may increase the workload on the heart, which may worsen the patient's clinical condition.]
(3) Patients with hyponatremia [The patient's clinical condition may be worsened.]
(4) Patients on dialysis or hemofiltration with serious renal disorder or azotemia [Urea and other amino acid metabolites may be retained.] (See section **2. Important Precautions**.)

2. Important Precautions

The volume of urea, etc. removed and accumulated in patients on dialysis or hemofiltration with serious renal disorder or azotemia varies depending on the dialysis method and patients' conditions. Initiation and continuation of administration should be determined after the patient's conditions are carefully checked based on assessment of blood biochemistry, acid-base equilibrium, and body-fluid balance, etc.

Amiparen 10% Contains *sodium bisulfite*, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. Sulfite sensitivity is seen more frequently in asthmatic than in non asthmatic people."

4.5. Undesirable effects

Reported incidences are based on 3973 patients, and a total of 35 (0.88%) patients experienced 39 adverse reactions including abnormal laboratory values. If adverse reactions are observed, discontinue the administration and institute appropriate treatment.

Reactions	**Frequency**		
	Unknown	**0.1% <5%**	**<0.1%**
Hypersensitivity	Rash etc.		
Gastrointestinal		Nausea, vomiting, etc.	
Cardiovascular	Chest discomfort, palpitation, etc.		
Hepatic		Increases in AST (GOT) or ALT (GPT)	Increase in total bilirubin
Renal		Increase in blood urea nitrogen	
Large dose and rapid administration	Acidosis		
Others	Chills, fever, feeling of warmth, headache		Vascular pain

Reporting suspected adverse reactions after authorization 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 via: Safety.reporting@egyptotsuka.com or by sending an e-mail to PV.followup@edaegypt.gov.eg

5. PHARMACOLOGICAL PROPERTIES

PHARMACOKINETICS

(Reference data in rats):

^{14}Carbon-labeled amino acids formulated in Amiparen® were readily distributed to plasma protein fractions after intravenous infusion in normal rats at 3, 7, and 57 weeks of age. The radioactivity was high in the protein fractions of the pancreas, liver, and kidneys and distributed rapidly in the muscles. The excretion of radioactivity into expired air over 72 hours post dosing accounted for 37.1% to 44.2% of the infused dose. The recovery rates in the urine and feces accounted for 3.9%–5.2% and 1.2%–3.1% of the infused dose, respectively. Urinary amino acid fractions contained only 1.1%–1.5% of the infused dose. The total retention of amino acids in the body amounted to more than 98.5% of the infused dose.

CLINICAL STUDIES

Clinical studies of Amiparen® 10% were conducted in a total of 546 surgical patients, mainly those who underwent gastrointestinal surgery. Amiparen® 10% was administered via the central vein (total parenteral nutrition) or via the peripheral vein (peripheral parenteral nutrition) after surgery. The results showed the high clinical value of Amiparen® 10% as a source of amino acids in terms of major protein metabolism-related parameters, including nitrogen balance, serum total protein and albumin levels, rapid protein turnover, and urinary excretion of 3-methylhistidine.

PHARMACOLOGY

The effect of Amiparen® 10% as a source of amino acids in total parenteral nutrition was assessed using normal rats and surgically stressed rats.

(1) Amiparen® 10% readily corrected and favorably maintained nitrogen balance, demonstrating a favorable nitrogen sparing effect in these animal models.

(2) Amiparen® 10% increased synthesis of plasma total protein and albumin.

(3) The urinary 3-methylhistidine/creatinine ratio as an indicator of protein catabolism in the muscle under stressed condition was low after Amiparen® 10% infusion, indicating a potent inhibitory effect on muscular protein breakdown.

(4) Plasma concentrations of free amino acids, including branched-chain amino acids, showed only minor fluctuation during Amiparen® 10% infusion, and amino acid metabolism was thought to be stable during Amiparen® 10% therapy.

Use in the Elderly

Because elderly patients often have reduced physiological function, it is advisable to consider reducing the dose by decreasing the infusion rate.

Pediatric Use

The safety of AMIPAREN Injection in low-birth-weight infants, neonates, and infants has not been established (insufficient clinical data).

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium Bisulfite* 0.2 g/L as an additive..
Glacial acetic acid used as a PH adjuster
Water for injection

6.2. Shelf life:

3 Years

6.3. Special precautions for handling and storage

1. Because an oxygen absorbent is enclosed between the bottle and the outer wrap to maintain stability of the solution, do not remove the outer wrap until use.
2. Do not use the product if the outer wrap covering the product has been damaged, the solution is discolored, or a precipitate that cannot be dissolved by shaking has formed.
3. Store at temperature not exceeding 30°C, use immediately after opening.
4. Do not use in case oxygen indicator tablet color changed from pink to purple or color of solution changed.
5. One single dose, Discard the remaining quantity in case the container not used completely.
6. Store at a temperature not exceeding 30°C, to be used immediately after opening.
7. Keep out of reach of children.
8. Do not puncture for ventilation during use.

6.4 Precautions Concerning Use

(1) Before administration

1) To minimize the risk of infection, carry out all procedures under aseptic conditions.
2) In cold environmental conditions, the solution should be warmed to near body temperature before use.
3) Use the solution immediately after opening the container. After use, discard all unused solution.

(2) During administration

1) The solution contains about 120 mEq/L of acetate. A large dose or concomitant use with an electrolyte solution requires careful monitoring of electrolyte balance.
2) Administer the solution slowly via a vein.
3) When vascular pain occurs, use an alternate site or discontinue the administration.

6.5. Nature and contents of container

1-outer carton box containing Low Density Polyethylene plastic bottle containing 250 ml or 500 ml solution closed with Natural (type 1) rubber cap (polyisoprene rubber+ kaoline+ sulfur) & immediate label enclosed in a gas barrier plastic bag (assembled of biaxially oriented polypropylene + adhesive + innovative barrier polyethylene terephthalate + linear low density polyethylene) with insert leaflet, ageless oxygen absorber & ageless eye oxygen indicator tablet.

2-**For tenders only:** outer carton box containing Low Density Polyethylene plastic bottle containing 100 ml or 200 ml solution closed with Natural (type 1) rubber cap (polyisoprene rubber+ kaoline+ sulfur) & immediate label enclosed in a gas barrier plastic bag (assembled of biaxially oriented polypropylene + adhesive + innovative barrier polyethylene terephthalate + linear low density polyethylene) with insert leaflet, ageless oxygen absorber & ageless eye oxygen indicator tablet.

6.6. Applicant name, Manufacturer & License holder Information

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