Totilac

Each 250ml of Totilac® infusion solution contains:

- Sodium lactate sol. (50%) 28.25 g (equal with 14.125 g Sodium lactate)
- Potassium chloride 0.075 g
- Calcium chloride 2H2O (100%) 0.05 g

Yielding:

<table>
<thead>
<tr>
<th></th>
<th>Mmol/L</th>
<th>meq/L</th>
<th>g/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na+</td>
<td>504.15</td>
<td>504.15</td>
<td>11.5</td>
</tr>
<tr>
<td>K+</td>
<td>4.02</td>
<td>4.02</td>
<td>0.16</td>
</tr>
<tr>
<td>Ca++</td>
<td>1.36</td>
<td>2.72</td>
<td>0.05</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>6.74</td>
<td>6.74</td>
<td>0.24</td>
</tr>
<tr>
<td>Lactate</td>
<td>504.15</td>
<td>504.15</td>
<td>44.92</td>
</tr>
</tbody>
</table>

Description

TOTILAC® is a sterile and non-pyrogenic solution containing hypertonic concentration of sodium lactate with physiological concentration of potassium chloride and calcium chloride in water for injection. This solution has an osmolarity of 1020 mOsml/L and a pH of ± 7.0.

Pharmacology

TOTILAC® contains strong ions which are fully dissociative into anions (lactate and chloride) and cations (sodium, potassium, calcium) when dissolved in water.

Sodium, a principal cation of extracellular fluid and its high concentration provides hypertonicity that is beneficial in fluid resuscitation as it improves hemodynamic with small volume.

Lactate, a physiological metabolite and acts as energetic substrate, which is actively oxidized by every mitochondrion-containing cell, i.e. the vast majority of cells in the body, especially in highly active organs such as brain, kidney, heart and muscles. Its oxidation results in energy release similar to that of glucose (4 Kcal/g of lactate).

Following a hypoxic period, lactate is a preferred or even an obligatory energy substrate over glucose because lactate acts as a ready to use substrate since its oxidation does not require investment of ATP, unlike glucose, and its usage prevent the reactive oxygen species (ROS) production.

Beside oxidation, lactate can be converted into glucose via gluconeogenic pathway, which occurs mainly in liver but also in kidney.

Calcium, it plays role in cardiac contractility.

Potassium, it prevents hypokalemia, which might be caused by sodium lactate infusion.
TOTILAC® solution is neutral (pH=7.0) and when lactate is metabolized, it doesn’t cause acidosis effect.

Post-coronary artery bypass graft

The safety and efficacy of Totilac® was evaluated in 208 patients, divided into 2 groups:

TOTILAC® and Ringer Lactate group. TOTILAC® was given at a max. dosage of 10 cc/kg BW over 12h while RL was given at a max. dosage of 30 cc/kg BW over 12h.

Efficacy: patients with TOTILAC® infusion, exhibited a better Cardiac Index (p=0.018) with less fluid infusion (p<0.0001) compared to that with RL group. The number of patients in TOTILAC® group required milrinone was significantly less compared to RL group (28% vs 39%, p<0.05).

Safety: the clinical safety profile was the same with RL, while hypernatremia event (plasma Na > 155 mmol/L) did not occur in this study.

Indications

Small volume fluid therapy for rapid restoration of intravascular volume (hemorrhagic shock, dengue shock, burnt patient, etc.); prevention of hypovolemia and maintaining stable hemodynamic status (perioperative condition); as an alternative in the treatment of metabolic acidosis, electrolyte disorder (hyponatremia); treatment for tissue/ peripheral edema; reduction of intracranial pressure in traumatic brain injury; source of alternative energy substrate during cell restoration post-ischemia.

Dosage and administration

- Dose is adjusted according to the individual need based on the status of patient’s haemodynamic.
- Intraoperative:
  - First loading of 3ml/kg BW in 15 minutes intravenously at the beginning of surgery.
  - Maintenance of 1.5 ml/kg BW/ hour during the surgery.
  - Second loading of 1.5 ml/kg BW in 15 minutes intravenously after protamine administration.
  - Post-operative:
    - Maximum dose 10cc/kg BW in 12 hours intravenously.
    - When the maximum dose of hypertonic sodium lactate solution is reached, it is permitted to infuse 6% hydroxyethyl starch (HES) in case of necessity of maintaining fluid therapy.

Contraindications

TOTILAC® is contraindicated in the states of hypovolemia and hypernatremia (plasma sodium is more than 155 mmol/L) and severe renal failure.

Warning and precautions

- Clinical evaluation and periodic laboratory determinations are necessary to monitor changes in fluid balance, electrolyte concentrations and acid base balance during prolonged parenteral therapy or whenever the condition of the patient warrants such evaluation.
- Solutions containing calcium ions should not be administered simultaneously through the same administration set as blood because of the likelihood of coagulation.
• Solutions which contain potassium should be used with great care in the presence of cardiac disease, particularly in digitalized patients, in patients with hyperkalemia, severe renal failure and in conditions in which potassium retention is present.
• Solutions containing sodium ions should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency and in clinical states in which there exist edema with sodium retention.
• In patients with diminished renal function, administration of solutions containing sodium or potassium ions may result in sodium or potassium retention.
• Solutions containing lactate ions should be used with great care in patients with metabolic or respiratory alkalosis as excess administration may result in metabolic alkalosis.
• The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentrations of such solutions.
• Do not administer unless solution is clear and container is undamaged. Discard unused portion.
• Hypertonic lactate is to be used with caution in patients with history of panic disorder since panic attacks have been reported with administration of lactate infusion.
• Used with caution in patients with diabetes and myasthenia gravis, hypertension and intestinal ulcers as well as in ion term treatment of babies and aged people.

Drug Interactions

TOTILAC® contains Ca++ ions. Precipitation may occur with the addition of anorganic phosphate, hydrogen carbonate or oxalate.

Carcinogenesis, mutagenesis

The active ingredients, potassium chloride, sodium chloride, calcium chloride and sodium lactate are neither carcinogenic nor mutagenic.

Adverse Reactions

Reactions which may occur because of the solution or the technique of administration include febrile response, infection, extravasation and hypervolemia. If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures and save the reminder of the fluid for examination if deemed necessary.

Overdosage

There is no overdose experience with TOTILAC® infusion. No specific antidotes to these preparations are known. Should overdose occur, treat the symptoms, and institute supportive measures as required.

Cautions:

Food, Drug, Devices and Cosmetics Act prohibits dispensing without prescription.

Availability

Infusion solution in flexy bag containing 250ml (DR-XY33427)

Manufactured by:
PT Finusolprima Farma International, Bekasi- Indonesia

For:

Innogene Kalbiotech Pte. Ltd.

Imported and Distributed by:

Delex Pharma International, Inc.