תאריך: אוקטובר 2019

רופא/ה, רוקח/ת נכבד/ה

חברת טבע מודיעה על העדכונים הבאים בעלון לרופא של התכשיר:

COMPOUND SODIUM LACTATE BP (HARTMANN'S SOLUTION)

SOLUTION FOR INFUSION

תרכובת סודיום לקטט BP (תמיסת הרטמן) תמיסה לאיפוזיה

Contains:

Sodium Chloride:	6.00 g/l
Potassium Chloride:	0.40 g/l
Calcium Chloride dihydrate:	0.27 g/l
Sodium Lactate:	3.20 g/l

עדכונים בעלון לרופא

<u>התוויה כפי שאושרה בתעודת הרישום:</u>

Source of water and electrolytes.
Regulation or maintenance of metabolic acidosis (except lactic acidosis).

<u>ברצוננו להודיע שהעלון לרופא עודכן, בפירוט שלהלן כלולים העדכונים העיקריים בלבד (תוספות מסומנות באדום והסרות מידע כטקסט מחוק):</u>

4.3. Contraindications

As for other calcium-containing infusion solutions, concomitant administration of ceftriaxone and Compound Sodium Lactate solution is contraindicated in newborns (≤28 days of age), even if separate infusion lines are used (risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream). For patients over 28 days of age please see section 4.4.

Compound Sodium Lactate solution is also contraindicated in patients with

- A known hypersensitivity to sodium lactate.
- Conditions associated with increased lactate levels (hyperlactataemia) including lactic acidosis, or impaired lactate utilization, such as severe hepatic insufficiency.

4.4.Special warnings and precautions for use

Hypersensitivity reactions
The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Incompatibilities

Ceftriaxone
In patients older than 28 days (including adults), ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions, including Compound Sodium Lactate solution, through the same infusion line. If the same infusion line is used for sequential administration, the line must be thoroughly flushed between infusions with a compatible fluid. For patients under 28 days please see section 4.3.

Electrolyte balance
Hypernatraemia
Compound Sodium Lactate solution should only be administered to patients with hypernatraemia after careful consideration of the underlying cause and alternative intravenous fluids. Monitoring of plasma sodium and volume status during treatment is recommended.
Compound Sodium Lactate solution should be administered with particular caution in patients with conditions predisposing to hypernatraemia (such as adrenocortical insufficiency, diabetes insipidus or extensive tissue injury) and in patients with cardiac disease.

Hyperchloraemia
Compound Sodium Lactate solution should only be administered to patients with hyperchloraemia after careful consideration of the underlying cause and alternative intravenous fluids. Monitoring of plasma chloride and acid-base balance during treatment is recommended.

Compound Sodium Lactate solution should be administered with particular caution to patients with conditions predisposing to hyperchloraemia (such as renal failure and renal tubular acidosis, diabetes insipidus), and patients with urinary diversion or patients taking certain diuretics (carbonic anhydrase inhibitors eg acetazolamide) or steroids (androgens, estrogens corticosteroids) and in patients with severe dehydration.

Fluid balance/renal function
Use in patients with renal impairment
Compound Sodium Lactate solution should be administered with particular caution to patients with renal impairment. In such patients administration of Compound Sodium Lactate solution may result in sodium and/or potassium retention.

Risk of Fluid and/or Solute Overload and Electrolyte Disturbances
Depending on the volume and rate of infusion, intravenous administration of Compound Sodium Lactate solution can cause

- fluid and/or solute overload resulting in overhydration and, for example, congested states, including pulmonary congestion and oedema.
- clinically relevant electrolyte disturbances and acid-base imbalance.

Clinical evaluation and periodic laboratory determinations may be necessary to monitor changes in fluid balance, electrolyte concentrations and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient or the rate of administration warrants such evaluation.
High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired hyponatraemia (see below).

Hyponatraemia
Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, post-operative stress, infections, burns, and CNS diseases), patients with heart-, liver- and kidney diseases and patients exposed to vasopressin agonists (see section 4.5) are at particular risk of acute hyponatraemia upon infusion of hypotonic fluids.

Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening brain injury.

Children, women in the fertile age and patients with reduced cerebral compliance (e.g. meningitis, intracranial bleeding, cerebral contusion and brain oedema) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatraemia.

Use in patients with hypervolaemia, overhydration or conditions causing sodium retention and oedema
Compound Sodium Lactate solution should be administered with particular caution to hypervolaemic or overhydrated patients.
Due to the sodium chloride content Compound Sodium Lactate solution should be administered with particular caution to patients with conditions that may cause sodium retention, fluid overload and oedema, such as patients with primary hyperaldosteronism, secondary hyperaldosteronism (associated with, e.g., hypertension, congestive heart failure, renal artery stenosis, or nephrosclerosis), or preeclampsia. (see also Section 4.5)

Acid-base balance
Use in patients at risk for alkalosis
Compound Sodium Lactate solution should be administered with particular caution to patients at risk for alkalosis. Because lactate is metabolized to bicarbonate, administration may result in, or worsen, metabolic alkalosis. Seizure may be precipitated by the alkalosis induced by lactate but this is uncommon.

Other warnings
Administration of citrate anticoagulated/preserved blood
Due to the risk of coagulation precipitated by its calcium content, Compound Sodium Lactate solution must not be added to or administered simultaneously through the same tubing with citrate anticoagulated/preserved blood.

Use in patients with type 2 diabetes
Lactate is a substrate for gluconeogenesis. Therefore glucose levels should be carefully monitored in patients receiving Compound Sodium Lactate.

Administration
Adding other medication or using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. In such case the infusion must be stopped immediately.

This medicinal product contains 301.3 mg sodium per 100 ml, equivalent to 15% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

This medicine contains 0.5 mmol (or 19.5 mg) potassium per 100 ml.

4.5.Interaction with other medicinal products and other forms of interaction

Ceftriaxone: See sections 4.3 and 4.4 for more information

Drugs leading to an increased vasopressin effect
The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hospital acquired hyponatraemia following inappropriately balanced treatment with i.v. fluids (see sections 4.2, 4.4 and 4.8).

- Drugs stimulating vasopressin release include: Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics
- Drugs potentiating vasopressin action include: Chlorpropamide, NSAIDs, cyclophosphamide
- Vasopressin analogues include: Desmopressin, oxytocin, terlipressin

Other medicinal products increasing the risk of hyponatraemia also include diuretics in general and antiepileptics such as oxcarbazepine.

Interaction related to the presence of potassium:
Because of its potassium content, Compound Sodium Lactate solution should be administered with caution in patients treated with agents or products that can cause hyperkalaemia or increase the risk of hyperkalaemia,

Interaction related to the presence of calcium:
Administration of calcium may increase the effects of digitalis and lead to serious or fatal cardiac arrhythmia. Therefore, larger volumes or a faster infusion rates should be used with caution in patients treated with digitalis glycosides.

Interaction related to the presence of lactate (which is metabolized into bicarbonate):
Caution is advised when administering Compound Sodium Lactate solution to patients treated with drugs for which renal elimination is pH dependent. Due to the alkalinizing action of lactate (formation of bicarbonate), Compound Sodium Lactate solution may interfere with the elimination of such drugs.

4.6. Fertility, pregnancy and lactation

Compound Sodium Lactate solution should be administrated with special caution for pregnant women during labour particularly as to serum-sodium if administered in combination with oxytocin (see section 4.4, 4.5 and 4.8).

4.8.Undesirable effects

The following adverse reactions (listed by MedDRA System Organ Class) have been reported spontaneously during the post-market experience.

Immune System Disorders	… Angioedema Blood pressure decreased, Respiratory distress, Dyspnea, Flushing, Throat irritation, Paresthesias, Hypoesthesia oral, Dysgeusia, Nausea, Pyrexia, Headache
Metabolism and Nutrition Disorders	Hyperkalaemia Hospital acquired hyponatraemia*
Nervous system disorders	Acute hyponatraemic encephalopathy*
General Disorders and Administration Site Conditions	… Infusion site swelling, Infusion site rash, Infusion site pruritus, Infusion site erythema, Infusion site burning

*Hospital acquired hyponatraemia may cause irreversible brain injury and death, due to development of acute hyponatraemic encephalopathy, frequency unknown (see sections 4.2. 4.4, 4.5).

The following adverse reactions have been reported spontaneously during the use of other sodium-lactate containing solutions:

- … Infusion site anesthesia (numbness)

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form

http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

6. PHARMACEUTICAL PARTICULARS

6.2.Incompatibilities

Ceftriaxone must not be mixed with calcium-containing solutions including Compound Sodium Lactate solution. See also sections 4.3 and 4.4.

Medications incompatible with Compound Sodium Lactate Solution
Ceftriaxone

6.3.Shelf life

Shelf life (Unopened): The expiry date of the product is indicated on the packaging materials