NEW ZEALAND DATA SHEET

1. Compound Sodium Lactate (Hartmann's)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Molecular formulae. Potassium chloride: KCl; sodium chloride: NaCl; calcium chloride dihydrate: $CaCl_2$; sodium S- lactate (chemical name, sodium 2-hydroxypropionate): $C_3H_5O_3Na$.

Sterile solution intended for intravenous use containing Sodium Lactate (3.17 g/L), Sodium Chloride (6.0 g/L), Potassium Chloride (400 mg/L) and Calcium Chloride Dihydrate (270 mg/L). Sodium Hydroxide and Hydrochloric acid is added for pH adjustment.

3. PHARMACEUTICAL FORM

The total amount of electrolytes per litre are: sodium 131 mmol, potassium 5 mmol, chloride 112 mmol, calcium 2 mmol, bicarbonate (as lactate) 28 mmol. The osmolality is approximately 255 mOsm/kg water.The solutions are isotonic, sterile, non-pyrogenic and do not contain antimicrobial agent or added buffers. The pH range is 5.0 to 7.0. Compound Sodium Lactate (Hartmann's) Solution for Injection is also known as Ringer-Lactate.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Compound Sodium Lactate (Hartmann's) is used:

- for intravenous fluid and electrolyte replacement
- as a source of bicarbonate in the treatment of mild to moderate metabolic acidosis associated with dehydration or associated with potassium deficiency
- as a vehicle for intravenous drug delivery, if the drugs are compatible with the solutions.

4.2 Dose and Method of Administration

To be used as directed by the physician. The dosage of Compound Sodium Lactate (Hartmann's) is dependent upon the age, weight and concomitant conditions of the patient as well as laboratory determinations and response.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration whenever solution and container permit as only sterile and non-pyrogenic equipment must be used for intravenous administration. Do not administer unless the solution is clear and the seal is intact.

As with all parental solutions compatibility with additives with the solution must be assessed before addition, by checking for a possible colour change and/or the appearance of the precipitates, insoluble complexes or crystals.

Before adding a substance or medication, verify that it is soluble and/or stable in water and that the pH range of Compound Sodium Lactate (Hartmanns) infusion solution is appropriate. Complete information is not available. Those

additives known to be incompatible should not be used. Consult with a pharmacist, if available. If in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced.

Contains no antimicrobials. For use in one patient on one occasion only. Discard any unused portion. Care should be taken with intravenous administration technique to avoid administration site reactions and infection.

4.3 Contraindications

- Known hypersensitivity to sodium lactate
- Congestive heart failure or severe impairment of renal function.
- Clinical states in which the administration of sodium and chloride is detrimental.
- concomitant administration of ceftriaxone in neonates (≤28 days of age) even if separate infusion lines are used
- concomitant administration of ceftriaxone in infants (>28 days of age), children and adults through same infusion line (e.g. via Y-connector)

4.4 Special Warnings and Precautions for Use

Compound Sodium Lactate (Hartmann's) is not for use in the treatment of lactic acidosis, severe metabolic acidosis or treatment of severe potassium deficiency. Although the solutions have potassium concentrations similar to that of plasma, it is insufficient to produce a useful effect in severe potassium deficiency.

The introduction of additives to any solution, regardless of type of container, requires special attention to ensure that no incompatibilities result. While some incompatibilities are readily observed, one must be aware that subtle physical, chemical and pharmacological incompatibilities can occur. The medical literature, the package insert and other available sources of information should be reviewed for thorough understanding of possible incompatibilities.

Concomitant administration with ceftriaxone in newborns (≤28 days of age) is not recommended through the same infusion line (see section **4.3 Contraindications**) due to the risk of fatal ceftriaxone calcium salt precipitation.

In patients older than 28 days (including adults), ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions, 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.

Do not administer Compound Sodium Lactate (Hartmanns) infusion solution unless it is clear and the seal is intact.

In a dilute condition, osmolarity is approximately equivalent to osmolality. Compound Sodium Lactate (Hartmann's) is isotonic. The addition of

potassium chloride (0.18%, 48mOsmol/L) to the Compound Sodium Lactate (Hartmanns) solution does not result in a hypertonic solution (324mOsmol/L). It is important to bear in mind that an administration of substantially hypertonic solution may lead to a wide variety of complications, such as crenation (shrinkage) of red blood cells and general cellular dehydration.

In patients with diminished renal function, administration of Compound Sodium Lactate (Hartmann's) may result in sodium, calcium and/or potassium retention. If a patient receives prolonged therapy, or the rate of administration warrants review, clinical evaluation and laboratory monitoring for changes in fluid balance, electrolyte concentration and acid/base balance should be conducted. Use with particular caution in patients with hyperkalaemia or risk of such (e.g. potassium excretion impairment, adrenocortical insufficiency, acute dehydration, severe renal impairement or extensive tissue injury or burns) and patients with cardiac disease administration of IV potassium can rapidly result in severe hyperkalaemia without symptoms, which may lead to fatal adverse reactions. Consideration should be given to withholding Compound Sodium Lactate (Hartmanns) infusion altogether in hypervolaemic or overhydrated patients, including those with severe renal impairment, primary or secondary hyperaldosteronism or preeclampsia, due to the risk of potassium and/or sodium retention, fluid overload and oedema.

The intravenous administration of Compound Sodium Lactate (Hartmanns) infusion solution can cause fluid and/or solute overloading resulting in dilution of the serum electrolyte concentrations, over-hydration, congested states, including pulmonary congestion and oedema, clinically relevant electrolyte disturbance and acid-base imbalance. The risk of dilution states is inversely proportional to the electrolyte concentrations of the injections. The risk of solute overload causing congested states with peripheral and pulmonary oedema is directly proportional to the electrolyte concentrations of the injections.

Compound Sodium Lactate (Hartmann's) should not be administered simultaneously with blood preparations through the same administration set, because of a possibility of coagulation.

The effect of the sodium lactate component in Compound Sodium Lactate (Hartmann's) on patients with metabolic or respiratory alkalosis should be monitored closely. Compound Sodium Lactate (Hartmann's) should be administered with extreme caution, if at all, in patients with increase lactate levels or impaired lactate utilisation such as cardiac disease, shock and severe hepatic insufficiency as alkalinisation may not be achieved and hyperlactaemia can develop (see also **Paediatric use** below).

Lactate is a substrate for gluconeogenesis so consideration should be given to the use of Compound Sodium Lactate (Hartmann's) infusion in Type 2 diabetics.

Patients with calcium renal calculi or a history of such, and patients with hypercalcaemia, or conditions predisposing to hypercalcaemia such as severe

renal impairment and granulomatous diseases associated with increased calcitriol synthesis including sarcoidosis, should use Compound Sodium Lactate (Hartmanns) infusion solution with caution.

Compound Sodium Lactate (Hartmann's) should be used with caution in patients receiving corticosteroids or corticotropin, i.e. potential sodium retention. Similarly with a patient receiving a potassium supplement preparation, as it may result in hyperkalaemia.

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.

Use in the elderly:
Clinical studies of Compound Sodium Lactate (Hartmann's) did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or drug therapy.

Paediatric Population:
Safety and effectiveness of Compound Sodium Lactate (Hartmann's) in paediatric patients have not been established by adequate and well controlled trials, however, the use of electrolyte solutions in the paediatric population is referenced in the medical literature. Lactate-containing solutions should be administered with particular caution to neonates and infants <6 months of age. The warnings, precautions and adverse reactions identified in the label copy should be observed in the paediatric population.

4.5 Interactions with other Medicines and other forms of Interaction

Compound Sodium Lactate (Hartmann's) should not be administered simultaneously with blood preparations through the same administration set, because of a possibility of coagulation.

Concomitant administration with ceftriaxone is not recommended through the same infusion line (see sections **4.3 Contraindications** and **4.4 Special Warnings and Precautions for Use**) due to the risk of fatal ceftriaxone-calcium salt precipitation.

Administration of calcium may increase the effects of digitalis and lead to serious or fatal cardiac arrhythmias. Therefore larger volumes or faster infusion rates should be used with caution in patients treated with digitalis glycosides.

Caution is advised when administering Compound Sodium Lactate (Hartmanns) infusion solution to patients treated with thiazide diuretics or vitamin D as these can increase the risk of hypercalcaemia.

Caution is advised when administering Compound Sodium Lactate (Hartmanns) infusion solution to patients treated with medicines that may increase the risk of sodium and fluid retention such as carbenoxolone and corticosteroids (see section **4.4 Special Warnings and Precautions for Use**).

Compound Sodium Lactate (Hartmanns) infusion solution may interfere with the elimination of medicines for which renal elimination is pH dependent. Renal clearance of acidic medicines such as salicylates, barbiturates and lithium may be increased. The renal clearance of alkaline medicines such as sympathomimetics (e.g. pseudoephedrine), dexamphetamine sulphate and fenfluramine hydrochloride may be decreased.

These products should not be administered concomitantly with potassium sparing diuretics (amiloride, spironolactone, triamterene), angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARAs) or the immunosuppressants tacrolimus and cyclosporin. Simultaneous administration of these medicines can result in severe hyperkalaemia, particularly in patients with severe renal insuficiency.

4.6 Fertility, Pregnancy and Lactation

Fertility:
Data not available.

Pregnancy:
There is no adequate data from the use of Compound Sodium Lactate (Hartmann's). The potential risks and benefits for each specific patient should be carefully considered before using Compound Sodium Lactate (Hartmann's) solution in pregnant women.

Breast feeding:
There is no adequate data from the use of Compound Sodium Lactate (Hartmann's) in lactating women. The potential risks and benefits of each specific patient should be carefully considered before using Compound Sodium Lactate (Hartmann's) solution in lactating women.

4.7 Effects on Ability to Drive and Use Machines

Data not available.

4.8 Undesirable Effects

Allergic reactions or anaphylactic/anaphylactoid symptoms such as localised or generalised urticaria, skin rash and erythema and itching/pruritus; skin swelling, periorbital, facial and/or laryngeal oedema (Quincke's oedema); chest tightness, chest pain, with tachycardia or bradycardia; nasal congestion, coughing, sneezing, bronchospasm and/or difficulty breathing have been reported during administration of Hartmann's Solution.

Adverse reactions may occur due to the solution or the technique of administration including fever response, or infection at the site of injection. Prolonged intravenous infusion of this type of product may cause venous thrombosis or phlebitis extending from the site of injection, extravasation, and hypervolaemia.

If an adverse reaction does occur, discontinue the infusion and evaluate the patient, institute appropriate therapeutic countermeasures, and save the remainder of the fluid for examination if deemed necessary.

Post-marketing Adverse Reactions
The following adverse reactions have been reported in the post-marketing experience:

IMMUNE SYSTEM DISORDERS: Hypersensitivity/infusion reactions, including Anaphylactic/Anaphylactoid reactions and the following manifestations:
Angioedema, chest pain, chest discomfort, decreased heart rate, tachycardia, blood pressure decreased, respiratory distress, bronchospasm, dyspnoea, cough, urticaria, rash, pruritus, erythema, flushing, throat irritation, paraesthesia's, hypoesthesia oral, dysgeusia, nausea, anxiety, pyrexia, headache.

METABOLISM AND NUTRITION DISORDERS: Hyperkalaemia

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Infusion site reactions, including phlebitis, infusion site inflammation, infusion site swelling, infusion site rash, infusion site pruritus, infusion site erythema, infusion site pain, infusion site burning.

Class Reactions
Other adverse reactions reported with Lactated Ringer's and 5% Dextrose Injection are:
Infusion site anaesthesia (numbness).

During administration of parenteral nutrition fat emulsions, two types of adverse reactions can occur.

Immediate reactions
At the beginning of the infusion, any of the following abnormal signs evoking a hypersensitivity reaction should be cause for immediate discontinuation of the infusion: sweating, shivering, cephalgia, dyspnoea.

Delayed reactions
During long-term parenteral nutrition of fat emulsions, the following adverse reactions have been observed:
Hepato-biliary disorders:

- increase of alkaline phosphatase, bilirubin and transaminases (ALT & AST)
- hepatomegaly
- icterus

Blood and lymphatic system disorders:

- thrombocytopenia

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/

4.9 Overdose

There is no overdose experience with Compound Sodium Lactate (Hartmanns) infusion solution. No specific antidotes to this preparation are known. Should overdose occur, treat the symptoms and institute appropriate supportive measures as required.

An excessive volume or too high a rate of administration may lead to fluid and sodium overload with a risk of oedema (peripheral and/or pulmonary), particularly when renal sodium excretion is impaired. Excessive administration of lactate may lead to metabolic alkalosis, which may be accompanied by hypokalaemia. Excessive administration of potassium may lead to the development of hyperkalaemia, especially in patients with severe renal impairment. Excessive administration of calcium salts may lead to hypercalcaemia.

When assessing an overdose, any additives in the solution must also be considered.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

A multiple electrolyte intravenous solution is intended for restoring the electrolyte balance and water for hydration. A combination of multiple electrolytes and sodium lactate, an alkalinising agent, will provide electrolyte balance and normalise the pH of the acid-base balance of the physiological system.

Sodium is the major cation of extracellular fluid and functions principally in the control of water distribution, fluid and electrolyte balance and osmotic pressure of body fluids. Chloride, the major extracellular anion, closely follows the physiologic disposition of the sodium cation in maintenance of the acid-base balance, isotonicity and electrodynamic characteristic of the cells.

In contrast to the sodium ion, potassium is a major cation of the intracellular fluid (160 mEq/L of intracellular water) and functions principally in the control of body fluid composition and electrolyte balance. Potassium participates in carbohydrate utilisation, protein synthesis and is critical in the regulation of nerve conduction and muscle contraction, particularly in the heart.

Calcium is essential for maintenance of the functional integrity of the nervous, muscular, and skeletal systems and cell membrane and capillary permeability. Calcium is the major component of the body skeleton. The calcium content in bone is continuously undergoing a process of resorption and formation. The normal concentration of calcium in plasma is between 2.2 and 2.6 mmol/L.

Sodium lactate is an alkalising agent. Lactate is slowly metabolised to bicarbonate and water. This reaction depends on the cellular oxidative activity. Under normal physiological conditions conversion of sodium lactate to bicarbonate requires about one to two hours. The bicarbonate metabolite then has similar actions to those of sodium bicarbonate preparations. That is, bicarbonate metabolites react with acid to produce carbon dioxide and water.

5.2 Pharmacokinetic Properties

As Compound Sodium Lactate (Hartmann's) is directly administered to the systemic circulation, the bioavailability (absorption) of the active components is complete (100%). Excess of calcium is predominantly excreted by the renal system, as in the case of potassium and sodium excretion.

5.3 Preclinical Safety Data

Carcinogenesis, mutagenesis, impairment of fertility:

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injection. Sodium Hydroxide and Hydrochloric acid is added for pH adjustment.

6.2 Incompatibilities

Additives may be incompatible. Complete information is not available. Those additives known to be incompatible should not be used. Consult with Pharmacist, if available. If, in the informed judgment of the doctor, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

6.3 Shelf life

3 years.

6.4 Special Precautions for Storage

Store at or below 25°C.

6.5 Nature and contents of container

Compound Sodium Lactate (Hartmann's) Solution for Injection in **free***flex*® bags;

Bag, 20 x 250mL	**5 L**
Bag, 30 x 250mL	**7.5 L**

Bag, 35 x 250mL	**8.75 L**
Bag, 40 x 250mL	**10 L**
Bag, 10 x 1000mL	**10 L**
Bag, 20 x 500mL	**10 L**

6.6 Special Precautions for Disposal
Any unused medicine or waste material should be disposed of in accordance with local requirements.

7 MEDICINE SCHEDULE
General Sales Medicine.

8. Sponsor
Fresenius Kabi New Zealand Limited
60 Pavilion Drive
Airport Oaks, Auckland, 2022
New Zealand
Freecall: 0800 144 892

9 DATE OF FIRST APPROVAL
10th May 2006

10 DATE OF REVISION OF THE TEXT
26 Sep 2018

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	New format
4.2	Additional safety related information regarding the addition of other products to this medicine
4.3	Additional contraindications included
4.4	Additional safety relation information inregards to warnings and precautions for the product
4.5	Additional safety related information included regarding interactions with other medicine
4.8	Post marketing adverse events included
4.9	Additional safety related information on potential over dosage included
6.5	Updated to reflect registration details