

AUSTRALIAN PRODUCT INFORMATION- COMPOUND SODIUM LACTATE (HARTMANN'S SOLUTION)

1 NAME OF MEDICINE

Calcium chloride dihydrate, potassium chloride, sodium chloride and sodium lactate.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Compound Sodium Lactate (Hartmann's) contains Sodium Lactate (3.17 g/L), Sodium Chloride (6.0 g/L), Potassium Chloride (400 mg/L) and Calcium Chloride Dihydrate (270 mg/L).

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.

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

3 PHARMACEUTICAL FORM

Injection for intravenous infusion.

The osmolality is approximately 255 mOsm/kg water. The solution is isotonic, sterile, non-pyrogenic and does 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's 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 doctor. The dosage of Compound Sodium Lactate (Hartmann's) is dependent upon the age, weight and clinical conditions of the patient as well as laboratory determinations.

Parenteral drug products should be inspected visually for particulate matter and discolouration prior to administration.

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.

Do not administer Compound Sodium Lactate (Hartmann's) unless the solution is clear and the seals are intact.

4.3 Contraindications

- Patients with a 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 (due to the risk of fatal ceftriaxone calcium salt precipitation in the neonate's bloodstream).
- 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.

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.

The medical literature, the package insert and other available sources of information should be reviewed for thorough understanding of possible incompatibilities.

Compound Sodium Lactate (Hartmann's) is isotonic (255mOsmol/kg). The addition of potassium chloride (0.18%) to Hartmann's solution does not result in a hypertonic solution (304 mOsmol/kg). 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 impairment or extensive tissue injury or burns) and patients with cardiac disease, as 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 (Hartmann's) 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 (Hartmann's) can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, 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.

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 increased lactate levels, impaired lactate utilisation such as cardiac disease, shock and severe hepatic insufficiency or otherwise at risk of alkalosis, as alkalinisation may not be achieved or metabolic alkalosis may worsen and hyperlactataemia can develop. Seizure may be precipitated by the alkalosis induced by lactate but this is uncommon.

Lactate is a substrate for gluconeogenesis so caution should be used with use of Compound Sodium Lactate (Hartmann's) 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 (Hartmann's) 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 Use:

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 precautions and adverse reactions identified for infants, children and adults should be observed in the paediatric population (see also section **4.5 Interactions with other medicines and other forms of interactions**).

Effects on laboratory tests

No data available.

4.5 Interaction with other medicines and other forms of interaction

Compound Sodium Lactate (Hartmann's) should not be administered simultaneously with blood preparations (e.g citrate anticoagulated/ preserved blood) 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 (Hartmann's) Infusion 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 (Hartmann's) to patients treated with medicines that may increase the risk of sodium and fluid retention such as carbenoxolone and corticosteroids (see **4.4 Special warnings and precautions for use**).

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

Compound Sodium Lactate (Hartmann's) 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 drugs can result in severe hyperkalaemia particularly in patients with severe renal insufficiency.

4.6 Fertility, pregnancy and lactation

Effects on fertility

Data not available.

Use in pregnancy (Category C)

There are no adequate data from the use of Compound Sodium Lactate (Hartmann's) in pregnant women.

Use in lactation

There are no adequate data from the use of Hartmann's IV and Modified Hartmann's IV Infusion in lactating women. The potential risks and benefits for each specific patient should be carefully considered before using Compound Sodium Lactate (Hartmann's) in lactating women.

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)

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, Paraesthesias, 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.

Reporting of 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 <https://www.tga.gov.au/reporting-problems>.

4.9 Overdose

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

Symptoms of overdosage with intravenous solutions are related to disturbed electrolyte levels and fluid imbalance. Symptoms indicative of overdose include shortness of breath, peripheral oedema, nausea, vomiting and diarrhoea, abdominal cramps, weakness, paraesthesia, paralysis, mental confusion, tachycardia and other cardiac abnormalities.

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.

Overdose requires immediate clinical assessment, cessation or slowing of intravenous fluids, laboratory assessment of electrolyte levels, calculation of fluid balance, ECG monitoring and commencement of appropriate supportive treatment.

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

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia) or 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

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 alkalinising 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.

Clinical trials

No data available.

5.2 Pharmacokinetic properties

Absorption

As Compound Sodium Lactate (Hartmann's) is directly administered to the systemic circulation, the bioavailability (absorption) of the active components is complete (100%).

Excretion

Excess of calcium is predominantly excreted by the renal system, as in the case of potassium and sodium excretion.

5.3 Preclinical safety data

Genotoxicity

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

Carcinogenicity

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. Do not reconnect partially used containers.

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

Compound Sodium Lactate (Hartmann's) Solution for Injection in **freeflex**[®] bags;

freeflex[®] bags

250mL AUST R: 148935

500mL AUST R: 29771

1000mL AUST R: 47410

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

Chemical structure

Molecular formulae. Potassium chloride: KCl; sodium chloride: NaCl; calcium chloride dihydrate: CaCl₂; sodium S- lactate (chemical name, sodium 2-hydroxypropionate): C₃H₅O₃Na.

CAS number

Sodium lactate - 867-56-1

Sodium chloride - 7647-14-5

Potassium chloride - 7447-40-7

Calcium chloride dihydrate - 10035-04-8

7 MEDICINE SCHEDULE (POISONS STANDARD)

Australia: Unscheduled

New Zealand: General Sales Medicine

8 SPONSOR

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10 May 2006

10 DATE OF REVISION OF THE TEXT

17 Jul 2018

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
	New format
4.3	Update to contraindications
4.4	Updates to precautions
4.5	Updates to interactions with other medicines
4.6	Update to use in pregnancy
4.8	Updates to adverse reactions
4.9	Update to overdose information