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 Solution) 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. 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 Solution) 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 Solution) 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 Solution) unless the solution is clear and the seals are intact.

4.3 CONTRAINDICATIONS

Compound Sodium Lactate (Hartmann's Solution) is contraindicated in 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.

As for other calcium-containing infusion solutions, concomitant administration of ceftriaxone and Hartmann's solution is contraindicated 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. In patients older than 28 days (including children and adults), ceftriaxone must not be administered simultaneously with IV calcium-containing solutions, including Hartmann's solution, through the same infusion line (e.g. via Y-connector).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Compound Sodium Lactate (Hartmann's Solution) is not for use in the treatment of lactic acidosis or severe metabolic acidosis. Although the Hartmann's solution has potassium concentrations similar to the concentration in plasma, it is insufficient to produce a useful effect in severe potassium deficiency, therefore it should not be used for treatment of 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 and other available sources of information should be reviewed for thorough understanding of possible incompatibilities.

Hartmann's solution is isotonic (255mOsmol/kg). The addition of potassium chloride (0.18%) to the Hartmann's solution does not result in a hypertonic solution (304 mOsmol/kg). It is important to bear in mind that administration of a 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 Hartmann's solution 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.

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.

Hyponatraemia

Monitoring of serum sodium is particularly important for hypotonic fluids. 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. Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (brain oedema) characterised by headache, nausea, seizures, lethargy and vomiting. Patients with brain oedema are at particular risk of severe, irreversible and life-threatening brain injury.

Fluid/solute overload and electrolyte disturbances

Depending on the volume and rate of infusion, the intravenous administration of Hartmann's solution 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.

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.

Use in patients with or at risk of hyperkalaemia

Hartmann's solution should be administered with particular caution, if at all, in patients with hyperkalaemia or conditions predisposing to hyperkalaemia (e.g. potassium excretion impairment, adrenocortical insufficiency, acute dehydration, severe renal impairment or extensive tissue injury or burns) and in patients with cardiac disease, as administration of IV potassium can rapidly result in severe hyperkalaemia without symptoms, which may lead to fatal adverse reactions.

Use in patients with hypervolaemia, overhydration, or conditions that cause sodium retention and oedema

Hartmann's solution should be administered with particular caution, if at all, in patients with conditions that may cause sodium retention, fluid overload and oedema. Consideration should be given to withholding Hartmann's solution 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.

Hartmann's solution should be used with caution in patients receiving corticosteroids or corticotropin, (i.e. potential sodium retention).

Use in patients with or at risk of alkalosis

Hartmann's solution should be administered with particular caution, if at all, to patients with alkalosis or at risk of alkalosis, because lactate is metabolised to bicarbonate and administration may result in, or worsen, metabolic alkalosis. The effect of the sodium lactate component in Hartmann's solution on patients with metabolic or respiratory alkalosis should be monitored closely.

Use in patients with or at risk of increased lactate levels or with impaired lactate utilisation

Hartmann's solution should be administered with extreme caution, if at all, in patients with conditions associated with increased lactate levels or impaired lactate utilisation such as cardiac disease, shock and severe hepatic insufficiency. Hyperlactataemia can develop in patients with severe hepatic insufficiency, since lactate metabolism may be impaired. In addition, Hartmann's solution may not produce alkalinising action in patients with severe hepatic insufficiency, since lactate metabolism may be impaired. Lactate-containing solutions should be administered with particular caution to neonates and infants less than 6 months of age (see also **Paediatric Use** below).

Use in patients with Type 2 diabetes

Lactate is a substrate for gluconeogenesis. This should be taken into account when Hartmann's solution is used in patients with Type 2 diabetes.

Use in patients with or at risk for hypercalcaemia

Solutions containing calcium salts, including Hartmann's solution should be used with caution in patients with:

- hypercalcaemia, or conditions predisposing to hypercalcaemia such as severe renal impairment and granulomatous diseases associated with increased calcitriol synthesis including sarcoidosis

- calcium renal calculi or a history of such calculi.

Use in the elderly

Clinical studies of Hartmann's solution 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 Hartmann's solution 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.

Effects on laboratory tests

No data available.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

Hartmann's solution should not be administered simultaneously with blood preparations (e.g citrate anticoagulated/preserved blood) through the same administration set, because of a possibility of the likelihood 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.

Caution is advised when administering Hartmann's solution to patients treated with 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 hyponatraemia following treatment with intravenous fluids (see **Section 4.4 SPECIAL WARNING AND PRECAUTIONS FOR USE**).

- Drugs stimulating vasopressin release such as chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors (SSRIs), 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, opioids.

- Drugs potentiating vasopressin action such as chlorpropamide, non-steroidal anti-inflammatories (NSAIDs), cyclophosphamide.

- Vasopressin analogues such as desmopressin, oxytocin, vasopressin, terlipressin.

Caution is advised when administering Hartmann's solution to patients treated with drugs that may increase the risk of hyponatraemia, such as diuretics and antiepileptics (e.g. oxcarbazepine).

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 Hartmann's solution to patients treated with thiazide diuretics or vitamin D as these can increase the risk of hypercalcaemia.

Caution is advised when administering Hartmann's 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**).

Caution is advised when administering Hartmann's solution to patients treated with drugs for which renal elimination is pH dependent. Due to the alkalinising action of lactate (formation of bicarbonate), Hartmann's solution may interfere with the elimination of such drugs:

- Renal clearance of acidic drugs such as salicylates, barbiturates and lithium may be increased.

- Renal clearance of alkaline medicines such as sympathomimetics (e.g. pseudoephedrine), dexamphetamine sulphate and fenfluramine hydrochloride may be decreased.

Hartmann's solution contains approximately 5 mmol/L potassium and caution is advised when administering Hartmann's solution to patients concomitantly being administered drugs that can cause hyperkalaemia or increase the risk of hyperkalaemia, such as potassium sparing diuretics (amiloride, spironolactone, triamterene), angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists (ARAs), the immunosuppressants tacrolimus and cyclosporin, or potassium supplement preparations. Simultaneous administration of these drugs can result in severe and potentially fatal hyperkalaemia, particularly in patients with severe renal insufficiency.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

Use in pregnancy (Category C)

There are no adequate data from the use of Hartmann's solution in pregnant women. The potential risks and benefits for each specific patient should be carefully considered before using Hartmann's solution in pregnant women.

Use in lactation

There are no adequate data from the use of Hartmann's solution in lactating women. The potential risks and benefits for each specific patient should be carefully considered before using Hartmann's solution 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, 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.

Other adverse reactions (Class reactions)

Other adverse reactions reported with similar products include:

- Hyponatraemia
- Hyponatraemic encephalopathy

- Infusion site anaesthesia (numbness) (reported with Lactated Ringer's and 5% Dextrose Injection).

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 Hartmann's solution. No specific antidotes to this preparation are known. Should overdose occur, treat the symptoms and institute appropriate supportive measures as required. The effects of an overdose may require immediate medical attention and treatment.

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 13 11 26 (Australia).

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 physiological 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 1 to 2 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 Hartmann's solution 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 not mutagenic.

Carcinogenicity

The active ingredients: potassium chloride, sodium chloride, calcium chloride and sodium lactate, are not carcinogenic.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

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

6.2 INCOMPATIBILITIES

Additives may be incompatible.. Those additives known to be incompatible should not be used (see **Section 4.2 DOSE AND METHOD OF ADMINISTRATION**).

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.

Ceftriaxone must not be mixed with calcium-containing solutions including Hartmann's solution (see **Sections 4.3 CONTRAINDICATIONS** and **4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

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. Store in a dry place.

6.5 NATURE AND CONTENTS OF CONTAINER

Compound Sodium Lactate (Hartmann's Solution) for Injection is supplied in **free***flex*® bags – polyolefin.

Compound Sodium Lactate (Hartmann's) 250 mL solution for injection bag AUST R: 148935 – available in packs of 20, 30, 35 and 40 bags.

Compound Sodium Lactate (Hartmann's Solution) 500 mL injection bag AUST R: 29771 – available in packs of 1 bag.

Compound Sodium Lactate (Hartmann's Solution) 1000 mL injection bag AUST R: 47410 – available in packs of 1 bag.

Not all pack sizes are marketed

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: $CaCl_2$; sodium S- lactate (chemical name, sodium 2-hydroxypropionate): $C_3H_5O_3Na$.

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)

Not scheduled

8 SPONSOR

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9 DATE OF FIRST APPROVAL

10 May 2006

10 DATE OF REVISION OF THE TEXT

12 October 2023

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
All	Minor editorial changes.
4.4	Updated safety data for hyponatraemia, fluid/solute overload and electrolyte disturbances, hyperkalaemia, alkalosis, impaired lactate utilisation, and hypercalcaemia.
4.5	Included safety data for vasopressin effects and hyperkalaemia.
4.6	Updated safety data for use in pregnancy.
4.8	Included safety information for class reactions.
4.9	Updated safety information for overdose.
6.2	Included ceftriaxone warning.
8	Updated sponsor details.