

PRODUCT INFORMATION

COMPOUND SODIUM LACTATE (HARTMANN'S) AND MODIFIED HARTMANN'S SOLUTION INTRAVENOUS INFUSION

NAME OF THE MEDICINE

Composition: the active ingredients in Hartmann's solution comprise sodium chloride (6g/L), sodium lactate (3.22g/L), potassium chloride (0.4g/L), and calcium chloride dihydrate (0.27g/L), whilst the modified Hartmann's solution contains the same compositions except potassium chloride is fortified (2.2g/L).

Chemical name/ molecular structure:

sodium lactate	$C_3H_5O_3Na$	or	$CH_3-CH(OH)-COONa$	or	sodium 2-hydroxypropionate
potassium chloride	KCl				
sodium chloride	NaCl				
calcium chloride	$CaCl_2$				

DESCRIPTION

Potassium chloride and sodium chloride occur as a colourless or white crystal and are freely soluble in water. Calcium chloride is a white, crystalline powder, hygroscopic and freely soluble in water. Sodium lactate is available as a sodium lactate solution having physical properties as a clear, colourless, slightly syrupy liquid, miscible with water.

The Compound Sodium Lactate solution (Hartmann's IV) and modified Hartmann's Intravenous Infusion are sterile, non-pyrogenic solutions. The only excipient in these solutions is water for injections; no antimicrobial agent or buffer is included. They are isotonic intravenous solutions with pH of 5.0 – 7.0 and osmolarities shown in Table 1 (see **Presentation and storage conditions**).

PHARMACOLOGY

Mechanism of Action:

A Multiple electrolyte intravenous solution is intended for restoring the electrolyte balance and water for hydration. A combination of multiple electrolyte and sodium lactate, alkalising 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 sodium cation in maintenance of acid-base balance, isotonicity and electrodynamic characteristic of the cells.

In contrast to sodium ion, potassium is a major cation of the intracellular fluid (160 mEq/liter 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 nervous, muscular, and skeletal system 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 to 2.6 mmol per litre.

Sodium lactate is an alkalisng agent. Lactate is slowly metabolised to bicarbonate and water. This reaction depends on the cellular oxidative activity. Under normal physiological condition conversion of sodium lactate to bicarbonate requires about 1 - 2 hours. The bicarbonate metabolite is then has a similar actions to those of sodium bicarbonate preparations. That is, bicarbonate metabolites react with acid to produce carbon dioxide and water.

Pharmacokinetics

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

INDICATIONS

The Hartmann's IV and Modified Hartmann's IV Infusion is indicated as a source of water and electrolytes. It is also used in patients as a source of bicarbonate in the treatment of mild to moderate metabolic acidosis associated with dehydration or associated with potassium deficiency. These solutions are indicated as methods of intravenous drug delivery, if the drugs are compatible with the solutions.

CONTRAINDICATIONS

The Hartmann's IV and Modified Hartmann's IV Infusion 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; 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 (eg. via Y-connector).

PRECAUTIONS

Hartmann's IV and its modified IV Infusion 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 safety of the Vialflex plastic container used in the Hartmann's IV and Modified Hartmann's IV Infusion has been confirmed in tests in animals according to the USP biological tests for plastic container, as well as by tissue culture toxicity studies. Solutions in contact with the plastic container can leach out certain of its chemical components in very small amounts within the expiration period, e.g., di-2-ethylhexyl phthalate (DEHP), up to 5 parts per million. Nevertheless, care should be exercised regarding possible incompatibility outcomes resulted either from the interaction between the plastic container or active ingredients and the added therapeutic substances. (See **Dosage and Administration**).

The introduction of additives to any solution, regardless of type of container, requires special attention to assure that no incompatibilities results. While some incompatibilities are readily observed, one must be aware that subtle physical, chemical and pharmacological incompatibilities can occur.

Concomitant administration with ceftriaxone in newborns (≤ 28 days of age) is not recommended through the same infusion line (see 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.

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

Do not administer the Hartmann's IV and Modified Hartmann's IV Infusion unless it is clear and seal is intact.

The Hartmann's IV Infusion is isotonic (254 mOsmol/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 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 the Hartmann's and Modified Hartmann's IV Infusion, 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 (eg 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 Hartmann's' and Modified Hartmann's IV 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 the Hartmann's IV and Modified Hartmann's IV Infusion 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.

The effect of sodium lactate component in the Hartmann's solution on patients with metabolic or respiratory alkalosis should be monitored closely. The Hartmann's IV and Modified Hartmann's IV Infusion should be administered with extreme caution, if at all, in patients with increased lactate levels or impaired lactate utilisation such as cardiac disease, shock and severe hepatic insufficiency as alkalisation may not be achieved and hyperlactaemia can develop (See also *Paediatric Use*).

Lactate is a substrate for gluconeogenesis so consideration should be given to the use of Hartmann's IV and Modified Hartmann's IV 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 Hartmann's IV and Modified Hartmann's IV Infusion with caution.

The Hartmann's IV and Modified Hartmann's IV Infusion should be used with caution in patients receiving corticosteroids or corticotropin, i.e., potential sodium retention. Similarly with a patient receiving 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 pregnancy (Category C)

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

Paediatric Use

Safety and effectiveness of Hartmann's IV and Modified Hartmann's IV Infusion 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.

Geriatric Use

Clinical studies of Hartmann's IV and Modified Hartmann's IV Infusion 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.

Genotoxicity/ Carcinogenicity

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

INTERACTIONS WITH OTHER MEDICINES

The Hartmann's IV and Modified Hartmann's IV Infusion should not be administered simultaneously with blood preparations (eg. 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 **Contraindications** and **Precautions**) 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 Hartmann's IV and Modified Hartmann's IV Infusion to patients treated with thiazide diuretics or vitamin D as these can increase the risk of hypercalcaemia.

Caution is advised when administering Hartmann's IV and Modified Hartmann's IV Infusion to patients treated with medicines that may increase the risk of sodium and fluid retention such as carbenoxolone and corticosteroids (see **Precautions**).

Hartmann's IV and Modified Hartmann's IV Infusion 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.

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 drugs can result in severe hyperkalaemia, particularly in patients with severe renal insufficiency.

ADVERSE EFFECTS

Allergic reactions or anaphylactic/anaphylactoid symptoms such as localized or generalized urticaria, skin rash & erythema and itching/pruritus; skin swelling, periobial facial and/or laryngeal edema (Quincke's edema); 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 IV and Hartmann's modified IV Infusion.

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, Dyspnea, Cough, Urticaria, Rash, Pruritus, Erythema, Flushing, Throat irritation, Paresthesias, 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% Glucose Injection are: Infusion site anaesthesia (numbness)

DOSAGE AND ADMINISTRATION

To be used as directed by the physician. The dosage of the Hartmann's IV and Modified Hartmann's IV Infusion is dependent upon the age, weight, concomitant treatments and clinical condition of the patient, as well as laboratory determinations and response. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit, as only sterile and nonpyrogenic equipment must be used for intravenous administration. As with all parenteral solutions, compatibility of the additives with the solution must be assessed before addition, by checking for a possible colour change and/or the appearance of 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 Hartmann's IV and Modified Hartmann's IV Infusion is appropriate. 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 physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. Refer to instructions below. Do not store solutions containing additives. Do not reconnect any partially used containers.

For modified Hartmann's IV infusion slow administration is recommended. The recommended administration rate should not exceed 20mmol/hour and not exceed 80mmol for a 24 hour period (= 6g KCl/24hr).

Direction for use of Viaflex plastic container

Do not use plastic containers in series connections. Such use could result in embolism due to residual air being drawn from the primary container before administration of the fluid from the secondary container is completed. Vented intravenous administration sets with the vent open, or pressurising intravenous solutions contained in flexible plastic containers to increase flow rate can also result in air embolism if the residual air in the container is not fully evacuated prior to administration.

To open:

Tear over wrap side at slit and remove solution container. Some opacity of the plastic due to moisture absorption during the sterilisation process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution as sterility may be impaired. If supplemental medication is desired, follow directions below.

Preparation for Administration:

(1) Suspend container from eyelet support. (2) Remove plastic protector from outlet port at the bottom of container. (3) Attach administration set.

To Add Medication: **Additives may be incompatible**

To add medication before solution administration: Prepare medication site. Using syringe with 19 to 22-gauge needle, puncture resealable medication port and inject. Mix solution and medication thoroughly. For high-density medication such as potassium chloride, squeeze ports while ports are upright and mix thoroughly.

To add medication during solution administration: Close clamp on the set. Prepare medication site. Using syringe with 19 to 22-gauge needle, puncture resealable medication port and inject. Remove container from IV pole and/or turn to upright position. Evaluate both ports by squeezing them while container is in the upright position. Mix solution and medication thoroughly. Return container to in use position and continue administration.

OVERDOSAGE

There is no overdose experience with the Hartmann's IV and Modified Hartmann's IV Infusion. 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 information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

PRESENTATION AND STORAGE CONDITIONS

The Hartmann's IV and Modified Hartmann's IV Infusion is supplied in Viaflex plastic containers as a single unit dose shown in the following Table.

Table 1: Compound Sodium, Lactate & modified HARTMANN's I.V. Infusions

Code No	Name of the active components [Concentrations (% , mmol/1000mL)]	Osmolarity (mOsmol/L)	ARTG/ AUSTR	Pack size (mL)
AHB2954	Potassium Chloride (0.22%, 29.5), Sodium Chloride (0.6%, 102.5), Sodium lactate (0.322 % , 28.75) & Calcium chloride (0.027%,1.84) [Modified Hartmann's]	329.0 (304.0)	19468	1000 (12's)
AHB2323	Potassium Chloride (0.04%, 5.4), Sodium Chloride (0.6%, 102.7), Sodium lactate (0.322%, 28.72) & Calcium Chloride (0.027%,1.84) [Hartmann's]	280.6 (254.0)	19425	500 (18's)
AHB2324	Potassium Chloride (0.04%, 5.4), Sodium Chloride (0.6%, 102.7), Sodium lactate (0.322%, 28.72) & Calcium Chloride (0.027%, 1.84) [Hartmann's]	280.6 (254.0)	48510	1000 (12's)

Note: Osmolarity is a calculated figure; whilst the figures in the brackets are Osmolality (mOsmol/kg).

Storage Condition

Store below 30°C.

Do not freeze

Exposure of pharmaceutical products to heat should be minimised. Avoid excessive heat.

NAME AND ADDRESS OF THE SPONSOR

Baxter Healthcare Pty Ltd
1 Baxter Drive
Old Toongabbie NSW 2146

POISON SCHEDULE OF THE MEDICINE

Unscheduled

DATE OF FIRST INCLUSION IN THE AUSTRALIA REGISTER OF THERAPEUTIC GOODS (ARTG)

30 September 1991

DATE OF MOST RECENT AMENDMENT

23 December 2014