

PRODUCT INFORMATION

COMPOUND SODIUM LACTATE (HARTMANN'S SOLUTION) AND 5% GLUCOSE INTRAVENOUS INFUSION

NAME OF THE MEDICINE

Composition: the ingredients in *Hartmann's solution and 5% glucose IV infusion* comprise sodium chloride (6 g/L), sodium lactate (3.22 g/L), potassium chloride (0.4g/L), calcium chloride dihydrate (0.27 g/L) and anhydrous glucose (50 g/L) in Water for Injections.

Chemical name	Molecular structure	Molecular mass	CAS number
sodium lactate	$C_3H_5NaO_3$	112.1	867-56-1
sodium chloride	NaCl	58.44	7647-14-5
potassium chloride	KCl	74.6	7447-40-7
calcium chloride (dihydrate)	$CaCl_2 \cdot 2H_2O$	147	10035-04-8
anhydrous glucose	$C_6H_{12}O_6$	180.2	50-99-7

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. Glucose is a monosaccharide, having physical characteristics as a white or almost white, crystalline powder, freely soluble in water, sparingly soluble in ethanol (96 per cent).

Hartmann's solution and 5% glucose IV infusions are sterile, non-pyrogenic solutions. There is no antimicrobial agent or buffer added. They are hypertonic intravenous solutions (osmolarity of 555 mOsmol/L) with pH of 4.0 - 6.5.

PHARMACOLOGY

Mechanism of Action:

A multiple electrolyte intravenous and glucose solution is intended for restoring the electrolyte balance as well as providing energy 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 alkalinising 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 then has similar actions to those of sodium bicarbonate preparations. That is, bicarbonate metabolites react with acid to produce carbon dioxide and water.

Glucose is readily metabolised into carbon dioxide and water, with a release of energy. As such, an administration of a glucose solution either by oral or parenteral route provides water for body hydration as well as calories. In addition, it may reduce catabolic loss of nitrogen from the body and aids in prevention of depletion of liver glycogen. That is, in the absence of glucose, amino acids undergo deamination. It is followed by oxidation, with a release of energy.

Pharmacokinetics

As *Hartmann's solution and 5% glucose IV infusion* is directly administered to the systemic circulation, the bioavailability (absorption) of the active components is complete (100%). Excess of calcium is predominantly excreted by renal system, as in the case of potassium and sodium excretion.

INDICATIONS

Hartmann's solution and 5% glucose 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

Hartmann's solution and 5% glucose IV infusion is contraindicated in patients with:

- known hypersensitivity to sodium lactate, or corn/corn products (because cornstarch is used as raw material for glucose production);
- 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 and 5% glucose IV infusion* is contraindicated in newborns (≤ 28 days of age), even if separate infusion lines are used (due to risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream).

In patients older than 28 days (including adults), ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions, including *Hartmann's solution and 5% glucose IV infusion*, through the same infusion line (e.g. via Y-connector).

PRECAUTIONS

Hartmann's solution and 5% glucose 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 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.

The safety of the Vialflex plastic container used in *Hartmann's solution and 5% glucose 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.

Due to the risk of coagulation precipitated by its calcium content, *Hartmann's solution and 5% glucose IV infusion* must not be added to or administered simultaneously through the same tubing with citrate anticoagulated/preserved blood (see **Interactions with Other Medicines**).

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 *Hartmann's solution and 5% glucose IV infusion* unless it is clear and seal is intact.

In a dilute condition, osmolarity is approximately equivalent to osmolality. *Hartmann's solution and 5% glucose IV infusion* is a hypertonic solution (555 mOsmol/L). It is important to bear in mind that an administration of substantially hypertonic solution may cause venous irritation, including phlebitis, and may lead to a wide variety of complications, such as crenation (shrinkage) of red blood cells and general cellular dehydration. Hyperosmolar solutions should be administered with caution, if at all, to patients with hyperosmolar states.

In patients with diminished renal function, administration of *Hartmann's solution and 5% glucose 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 solution and 5% glucose 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 *Hartmann's solution and 5% glucose 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 *Hartmann's solution and 5% glucose IV infusion* on patients with metabolic or respiratory alkalosis should be monitored closely. *Hartmann's solution and 5% glucose IV infusion* 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 alkalisation 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.

Solutions containing glucose should be used with caution in patients with impaired glucose tolerance or diabetes mellitus. Lactate is a substrate for gluconeogenesis so caution should be used with *Hartmann's solution and 5% glucose IV infusion* in Type 2 diabetics. As *Hartmann's solution and 5% glucose IV infusion* contains glucose and lactate (which is metabolised to glucose), administration that exceeds the metabolic capacity for glucose may lead to hyperglycaemia.

Hyperglycaemia has been implicated in increasing cerebral ischaemic brain damage and impairing recovery after acute ischaemic strokes. Caution is recommended in using glucose-containing solutions in such patients. Early hyperglycaemia has also been associated with poor outcomes in patients with severe traumatic brain injury. Glucose-containing solutions should therefore be used with caution in patients with head injury, in particular during the first 24 hours following the trauma.

If hyperglycaemia occurs, the rate of glucose administration should be reduced and/or insulin administered, or the insulin dose adjusted.

Solutions containing calcium salts (including *Hartmann's solution and 5% glucose IV infusion*) should be used with caution in patients with:

- hypercalcaemia or conditions predisposing to hypercalcaemia, such as patients with severe renal impairment and granulomatous diseases associated with increased calcitriol synthesis such as sarcoidosis
- calcium renal calculi or a history of such calculi.

Hartmann's solution and 5% glucose 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.

Use in pregnancy (Category C)

There are no adequate data from the use of *Hartmann's solution and 5% glucose IV infusion* in pregnant women. The potential risks and benefits for each specific patient should be carefully considered before using *Hartmann's solution and 5% glucose IV infusion* in pregnant women.

Use in lactation

There are no adequate data from the use of *Hartmann's solution and 5% glucose IV infusion* in lactating women. The potential risks and benefits for each specific patient should be carefully considered before using *Hartmann's solution and 5% glucose IV infusion* in lactating women.

Paediatric Use

Safety and effectiveness of *Hartmann's solution and 5% glucose 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. Plasma electrolyte concentrations should be closely monitored in the paediatric population.

Lactate-containing solutions should be administered with particular caution to neonates and infants <6 months of age.

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient and concomitant therapy, and should be determined by the consulting physician experienced in paediatric intravenous fluid therapy.

Newborns – especially those born premature and with low birth weight - are at increased risk of developing hypo- or hyperglycaemia and therefore need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycaemic control in order to avoid potential long term adverse effects. Hypoglycaemia in the newborn can cause prolonged seizures, coma and brain damage. Hyperglycaemia has been associated with intraventricular haemorrhage, late onset bacterial and fungal infection, retinopathy of prematurity, necrotising enterocolitis, bronchopulmonary dysplasia, prolonged length of hospital stay, and death.

Geriatric Use

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 and glucose are neither carcinogenic nor mutagenic.

INTERACTIONS WITH OTHER MEDICINES

Hartmann's solution and 5% glucose 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.

Use of intravenous infusions containing glucose may necessitate review of a patient's oral hypoglycaemic or insulin requirements. Close monitoring of serum glucose may be required.

Concomitant administration with ceftriaxone is not recommended through the same infusion line (see **Contraindications**) 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 solution and 5% glucose IV infusion* to patients treated with:

- thiazide diuretics or vitamin D as these can increase the risk of hypercalcaemia
- medicines that may increase the risk of sodium and fluid retention such as carbenoxolone and corticosteroids
- medicines for which renal elimination is pH dependent. Due to the alkalinising action of lactate (formation of bicarbonate), *Hartmann's solution and 5% glucose IV infusion* 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 (eg. pseudoephedrine), dexamphetamine sulphate and fenfluramine hydrochloride may be decreased.

Hartmann's solution and 5% glucose IV infusion 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 and potentially fatal hyperkalaemia, particularly in patients with severe renal insufficiency.

ADVERSE EFFECTS

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, bronchospasm, dyspnoea, cough, urticaria, rash, pruritus, erythema, nausea, pyrexia.

General Disorders and administration site conditions:

Infusion site reactions, including infusion site pruritus, infusion site erythema and infusion site anaesthesia (numbness).

Other Reactions:

Other adverse reactions reported with Lactated Ringer's Injection (without Glucose) and Sodium Lactate Injection are:

- Other manifestations of hypersensitivity/infusion reactions:
Decreased heart rate, tachycardia, blood pressure decreased, respiratory distress, flushing, throat irritation, paresthesias, hypoesthesia oral, dysgeusia, anxiety, headache
- Hyperkalaemia

- Other infusion site reactions:
Phlebitis, infusion site inflammation, Infusion site swelling, Infusion site rash, infusion site pain, infusion site burning.

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.

DOSAGE AND ADMINISTRATION

To be used as directed by the physician. The dosage of *Hartmann's solution and 5% glucose IV infusion* is dependent upon the age, weight, concomitant treatments and clinical condition of the patient, as well as laboratory determinations and response.

The infusion rate should not exceed the patient's ability to utilise glucose in order to avoid hyperglycaemia. The infusion rate of intravenous solutions containing glucose should be selected with caution in children (see *Paediatric Use*).

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. Do not administer unless the solution is clear and the seal is intact.

As with all parenteral solutions, compatibility of the additives with the solution must be assessed before addition. Before adding a substance or medication, verify that it is soluble and/or stable in water and that the pH range of *Hartmann's solution and 5% glucose IV infusion* is appropriate. After addition, check for a possible colour change and/or the appearance of precipitates, insoluble complexes or crystals.

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. Solutions containing additives should be used immediately, and not stored. Do not reconnect any partially used containers.

The product should be used for one patient on one occasion only. Any unused portion should be discarded.

Direction for use of Viaflex plastic container

Do not remove unit from over-wrap until ready for use. The inner bag maintains the sterility of the product. 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 down 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 *Hartmann's solution and 5% glucose IV infusion*. No specific antidotes to this preparation are known. Should overdose occur, immediate medical attention may be required to treat the symptoms and to institute appropriate supportive measures.

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. Excessive administration of glucose may lead to hyperglycaemia, hyperosmolarity, osmotic diuresis, and dehydration.

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

Hartmann's solution and 5% glucose IV infusion is supplied in Viaflex plastic containers as a single unit dose (see Table 1).

Table 1: Compound Sodium Lactate (Hartmann's Solution) and 5% Glucose IV Infusion

Code No	Name of the active components [Concentrations (% , mmol/1000mL)]	Osmolarity (mOsmol/L)	ARTG/ AUST R	Pack size* (mL)
AHB2073	Potassium Chloride (0.04%, 5.4), Sodium Chloride (0.6%, 102), Sodium Lactate (0.322%, 28.7) Calcium Chloride dehydrate (0.027%, 2) Glucose (5%, 278)	555	19422	500
AHB2074	Potassium Chloride (0.04%, 5.4), Sodium Chloride (0.6%, 102), Sodium Lactate (0.322%, 28.7) Calcium Chloride dehydrate (0.027%, 2) Glucose (5%, 278)	555	48490	1000

*not all pack sizes are marketed.

Note: Osmolarity is a calculated figure; in a dilute condition, osmolarity/L is approximately equivalent to Osmolality (mOsmol/kg).

Storage: Exposure of pharmaceutical products to heat should be minimised. Avoid excessive heat. It is recommended that the product be stored below 30°C.

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

06 March 2015