Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Hartmann's Solution for Infusion, PSEB bag

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Bag :	50 ml	100 ml	250 ml	500 ml	1000 ml
Sodium chloride (g)	0.30	0.60	1.50	3.00	6.00
Potassium chloride (g)	0.020	0.040	0.10	0.20	0.40
Dihydrated calcium chloride (g)	0.01	0.03	0.07	0.14	0.27
50% sodium lactate solution (g)	0.32	0.63	1.59	3.17	6.34

For full list of excipients, see section 6.1.

Molar formula

Bag :	50 ml	100 ml	250 ml	500 ml	1000 ml
Sodium (mmol)	6.55	13.09	32.73	65.45	130.90
Potassium (mmol)	0.27	0.54	1.35	2.70	5.40
Calcium (mmol)	0.09	0.18	0.46	0.92	1.84
Chloride (mmol)	5.59	11.17	27.93	55.85	111.70
Lactate (mmol)	1.42	2.83	7.08	14.15	28.30

3 PHARMACEUTICAL FORM

Solution for infusion.
Osmolarity: 279 mOsm/l
Osmolarity: 255 mOsm/kg
pH: 5.5 to 6.3
Clear colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

- Predominantly extracellular dehydration, regardless of cause (vomiting, diarrhea, fistulas, etc.).
- Hypovolemia regardless of cause: hemorrhagic shock, burns, peri-operative water and electrolyte loss.
- Mild metabolic acidosis.

4.2 Posology and method of administration

Posology:
This is determined by the physician according to clinical status, age and weight of the patient and according to laboratory findings.

Method of administration:
This solution must be given by slow intravenous infusion under strictly aseptic conditions.

Fluid balance, serum electrolytes and acid-base balance may need to be monitored before and during administration, with particular attention to serum sodium in patients with increased non-osmotic vasopressin release (syndrome of inappropriate antidiuretic hormone secretion, SIADH) and in patients co-medicated with vasopressin agonist drugs, due to the risk of hospital acquired hyponatraemia (see sections 4.4, 4.5 and 4.8).
Monitoring of serum sodium is particularly important for products with lower sodium concentration compared to serum sodium concentration.

Paediatric patients:

The infusion rate and volume depend on the age, weight, clinical condition (e.g. burns, surgery, head-injury, infections), and concomitant therapy and should be determinded by the consulting physician experienced in paediatric intravenous fluid therapy (see section 4.4 and 4.8)

4.3 Contraindications

This medicine is contraindicated in the following situations :
- Hypervolaemia (predominantly extracellular hyperhydration),
- decompensated congestive cardiac failure,
- hyperkalemia,
- hypercalcemia,
- metabolic alkalosis,
as well as in combination with digitalis (see "Interaction with other medicinal products and other forms of interaction" section).

4.4 Special warnings and precautions for use

Warnings
This solution must not be given by intramuscular injection.

Keep to a slow infusion rate.
The infusion must be stopped if any abnormal sign develops.

Risk of complications related to volume and amount of electrolytes administered.
Risk of overload of cardiovascular system with pulmonary edema, especially in predisposed individuals.

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 (see below).

Hyponatraemia:
Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, post-operative stress, infections, burns, and CNS diseases), patients with heart-, liver- and kidney diseases and patients exposed to vasopressin agonists (see section 4.5) are at particular risk of acute hyponatraemia upon infusion of hypotonic fluids.

Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening brain injury.

Children, women in fertile age and patients with reduced cerebral compliance (e.g. meningitis, intracranial bleeding, cerebral contusion and brain oedema) are at particular risk of the severe and life-threatening complications, because these patients are particularly vulnerable to the effects of brain swelling caused by acute hyponatraemia.

Infusion of Hartmann's solution may cause metabolic alkalosis because of the presence of lactate ions.
Hartmann's may not produce its alkalinizing action in patients with hepatocellular insufficiency since lactate metabolism may be impaired.

Check the color and clarity of the solution, as well as that the container is not damaged before use. Discard any damaged or partially used container.
In case of concomitant blood transfusion and because of the presence of calcium, Hartmann's solution must not be administered via the same infusion system because of the risk of coagulation.

Precautions for use
The patient's clinical status and laboratory parameters (blood and urine electrolytes) must be monitored during use of this solution, especially in the following situations:
- congestive cardiac failure,
- severely impaired renal function,
- edema with sodium retention.

Since this solution contains potassium, combination with hyperkalaemic diuretics is not recommended, plasma potassium must be particularly closely monitored in patients at risk of hyperkalemia, e.g. in the presence of severe chronic renal failure.

It is inadvisable to use this medicine in combination with angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists, or with tacrolimus (see "Interaction with other medicinal products and other forms of interaction" section).
Precautions for using bag:
- use immediately once opened;
- do not use an air entry;
- do not connect in series since the residual of the first container might be carried on by the solution coming from the second container, with the risk of air embolism.

4.5 Interaction with other medicinal products and other forms of interactions

Drugs leading to an increased vasopressin effect
The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and increase the risk of hospital acquired hyponatraemia following inappropriately balanced treatment with i.v. fluids (see sections 4.2, 4.4 and 4.8).

- Drugs stimulating vasopressin release, e.g.: Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics
- Drugs potentiating vasopressin action, e.g.: Chlorpropamide, NSAIDs, cyclophosphamide
- Vasopressin analogues, e.g.: Desmopressin, oxytocin, vasopressin, terlipressin

Other medicinal products increasing the risk of hyponatraemia also include diuretics in general and antiepileptics such as oxcarbazepine.

Interactions related to the presence of calcium
Contraindicated combination:
+ digitalis preparations : serious or even fatal cardiac arrhythmias, especially in the presence of hypokalemia.

- ***Combination needing to be taken into account:***
+ thiazide diuretics: risk of hypercalcemia via decreased urinary calcium excretion.

Interactions related to the presence of potassium
- ***Inadvisable combinations:***
+ hyperkalemic diuretics: amiloride, spironolactone, triamterene, alone or in association : potentially fatal hyperkalemia, notably in the presence of renal failure (addition of hyperkalemic effects).

+ angiotensin converting enzyme inhibitors (ACEi) and, by extrapolation, angiotensin II receptor antagonists: potentially fatal hyperkalemia, notably in the presence of renal failure (addition of hyperkalemic effects).

+ tacrolimus: potentially fatal hyperkalemia, notably in the presence of renal failure (addition of hyperkalemic effects).

4.6 Fertility, pregnancy and lactation

This solution can be used during pregnancy or lactation if necessary.
RINGER LACTATE FRESENIUS should be administrated with special caution for pregnant women during labour particularly as to serum-sodium if administered in combination with oxytocin (see section 4.4, 4.5 and 4.8).

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

Potential undesirable effects may occur in poor conditions of use or if administration is too fast.

During administration of Hartmann's Solution for Infusion, the following undesirable effects have been reported:

- General disorders and administration site conditions: oedema due to water/sodium overload (unknown frequency).
- Metabolism and nutrition disorders: Hospital acquired hyponatremia*
- Nervous system disorders : Acute hyponatremic encephalopathy*

*Hospital acquired hyponatraemia may cause irreversible brain injury and death, due to development of acute hyponatraemic encephalopathy, frequency unknown (see sections 4.2. 4.4, 4.5).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorization 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 in Ireland to HPRA Pharmacovigilance
Kevin O'Malley House
Earlsfort Centre
Earlsfort Terrace
IRL-Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
medsafety@hpra.ie

4.9 Overdose

Poor conditions of use, such as an overdose, may lead to signs of hypervolemia with tightened skin, venous stasis, oedema – possibly also lung – or brain oedema, disturbed acid-base balance and electrolyte balance and serum hyperosmolarity.

The infusion should be interrupted immediately.

Overdose should be treated in a specialist unit.

Extra-renal dialysis may be necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Solution Modifying Electrolyte Balance

ATC Code: BO5 BB 01

This is an isotonic crystalloid solution to be used for vascular filling and restoration of water/electrolyte balance and which has an ionic composition very close to that of extracellular fluid.

The correction of extracellular dehydration and/or of blood volume deficit is accompanied by hemodilution.

Pharmacological properties are those of the constituents of the solution (sodium, potassium, calcium, chloride).
Hartmann's Solution for Infusion is neutral and has an excess of chloride ions over sodium ions because of the presence of potassium chloride and calcium chloride.

Lactate ion is a bicarbonate precursor buffer anion, i.e. participating in the regulation of acid-base balance. This conversion may be impaired in the presence of hepatocellular insufficiency.

Metabolic alkalosis may result from excess intake of lactate ions.

If lactate metabolism is blocked (type B lactic acidosis), the intake of lactate results in accumulation of the anion in the blood.

In contrast, during the correction of hypovolemic shock (with type A lactic acidosis), improvement in circulatory status, and hence in hepatic perfusion, enables the restoration of normal lactate metabolism which corrects the process.

5.2 Pharmacokinetic properties

This solution disseminates in the extracellular compartment, with a matching increase in the volume of the latter. Lactate ion is quickly metabolized by the liver, where it is converted to pyruvate, used in the Krebs cycle with the production of bicarbonate.

5.3 Preclinical safety data

Non clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Hydrochloric acid (pH adjustment)
Sodium hydroxide (pH adjustment)
Water for injections

6.2 Incompatibilities

Physical-chemical incompatibilities:

It is up to the physician to determine the incompatibility of an added medicine regarding Hartmann's solution, by checking for any possible color change and/or possible formation of precipitate, insoluble complex or crystals.

There is physical-chemical incompatibility with certain antibiotics when they are given intravenously: chlortetracycline, amphotericin B, oxytetracycline.

Before adding any medicine, check that the pH zone in which it is effective corresponds to that of Hartmann's Solution for Infusion.
Also check the package leaflet of the medicine to be added.

Once a medicine is added to Hartmann's Solution for Infusion, the mixture must be administered immediately.

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years for polypropylene/styrene, ethylene, butadiene bags, with or without outer packaging.

2 years for polypropylene/SIS- polypropylene/SEB bags with outer packaging (50 ml, 100 ml, 250 ml, 500 ml and 1000 ml).

After opening or mixture with other drugs, the product should be used immediately.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

1 and 20 x 250 ml, 1 and 15 x 500 ml or 1 and 8 x 1000 ml in polypropylene/styrene, ethylene, butadiene bag with overwrap.

1 and 40 x 250 ml, 1 and 20 x 500 ml or 1 and 10 x 1000 ml in polypropylene/styrene, ethylene, butadiene bag without overwrap.

Polypropylene/styrene-isopprene-styrene polypropylene/styrene-ethylene-butadiene bag with an overwrap.

1 x 50ml, 40 x 50 ml, 60 x 50 ml, 65 x 50 ml, 70 x 50 ml.
1 x 100 ml, 40 x 100 ml, 50 x 100 ml, 55 x 100ml, 60 x 100 ml.
1 x 250ml, 20 x 250 ml, 30 x 250 ml, 35 x 250 ml, 40 x 250 ml.
1 x 500 ml, 15 x 500 ml, 20 x 500 ml.
1 x 1000 ml, 8 x 1000 ml, 10 x 1000 ml.

1, 40, 60, 65, 70 x 50 ml, 1, 40, 50, 55, 60 x 100 ml, 1, 20, 30, 35, 40 x 250 ml, 1, 15, 20 x 500 ml and 1, 8, 10 x 1000 ml in polypropylene/SIS-polypropylene/SEB bags with overwrap.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Check the color and clarity of the solution, as well as that the container is not damaged before use. Discard any damaged or partially used container.

Precautions for using bag:

- use immediately once opened;
- do not use an air entry;
- do not connect in series since the residual of the first container might be carried on by the solution coming from the second container, with the risk of air embolism.

The chemical and physical stability of any additive at the pH of solution Hartmann's, introduced into the Hartmann's, must be established before use.

Once a medicine is added to Hartmann's Solution for Infusion, the mixture must be administered immediately.

7 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1
Bad Homburg v.d.H 61352
Germany

8 MARKETING AUTHORISATION NUMBER

PA2059/057/002

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10 DATE OF REVISION OF THE TEXT

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