Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Hemosol B0 solution for haemodialysis/haemofiltration

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Hemosol B0 consists of a two compartment polyolefin bag containing the electrolyte solution in the small compartment (compartment A) and the buffer solution in the large compartment (compartment B).

BEFORE RECONSTITUTION

1 000 ml of electrolyte solution (small compartment A) contains: active substances:	
Calcium chloride, $2H_2O$	5,145 g
Magnesium chloride, $6H_2O$	2,033 g
Lactic acid	5,4 g
1 000 ml of buffer solution (large compartment B) contains: active substances:	
Sodium hydrogen carbonate	3,09 g
Sodium chloride	6,45 g

AFTER RECONSTITUTION

The small and the large compartments are mixed to give one reconstituted solution whose ionic composition is:

	in mmol/l	**in mEq/l**
Calcium Ca^{2+}	1,75	3,50
Magnesium Mg^{2+}	0,5	1,0
Sodium Na^{+}	140	140
Chloride Cl^{-}	109,5	109,5
Lactate	3	3
Hydrogen carbonate HCO_3^{-}	32	32

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for haemodialysis/haemofiltration.
Clear and colourless reconstituted solution.

Theoretical Osmolarity: 287 mOsm/l

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

As substitution solution in continuous haemofiltration and haemodiafiltration and as dialysis solution in continuous haemodialysis for acute renal failure in adult and children of all ages.

4.2 Posology and method of administration

Posology:

The rate at which Hemosol B0 is administered depends on the blood concentration of electrolytes, acid-base balance, fluid balance and overall clinical condition of the patient. The volume of replacement solution and/or dialysate to be administered will also depend on the desired intensity (dose) of the treatment. The solution should be prescribed and administration (dose, infusion rate, and cumulative volume) should be established only by a physician experienced in critical care medicine and CRRT (Continuous Renal Replacement Therapy).
Commonly used flow rates for the substitution solution in haemofiltration and haemodiafiltration are:
Adult: 500 - 3000 mL/hour

Commonly used flow rates for the dialysis solution (dialysate) in continuous haemodialysis are:
Adult: 500 - 2500 mL/hour

Commonly used flow rates in adults are approximately 2000 to 2500 ml/h which correspond to a daily fluid volume of approximately 48 to 60 L.

Special population:

Elderly population
Evidence from clinical studies and experience suggests that use in the elderly population is not associated with differences in safety or effectiveness.

Paediatric population:

The range of flow rates for the substitution solution in haemofiltration and haemodiafiltration and for the dialysis solution (dialysate) in continuous haemodialysis are:
Children (from neonates to adolescents to 18 years): 1000 to 2000 mL/h/1.73 m^2
Flow rates up to 4,000 mL/h/1.73 m^2 may be needed, especially in younger children (≤10 kg). The absolute flow rate (in mL/h) in the paediatric population should generally not exceed the maximum adult flow rate.

Method of administration:
Intravenous use and for haemodialysis.

Hemosol B0, when used as a substitution solution is administered into the extracorporeal circuit before (pre-dilution) or after the haemofilter or haemodiafilter (post-dilution).

For instructions on reconstitution of the medicinal product before administration, see section 6.6.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Warnings:

The substitution solution Hemosol B0 is potassium-free. The serum potassium concentration must be monitored before and during hemofiltration and/or hemodialysis.
The electrolyte solution **must** be mixed with the buffer solution **before use** to obtain the final solution suitable for haemofiltration/haemodiafiltration/continuous haemodialysis.

Use only with appropriate extracorporeal renal replacement equipment.

Because the solution contains no glucose, administration may lead to hypoglycemia. Blood glucose levels should be monitored regularly.

Hemosol B0 contains hydrogen carbonate (bicarbonate), and lactate (a hydrogen carbonate precursor) which can influence the patient's acid–base balance. If metabolic alkalosis develops or worsens during therapy with the solution, the administration rate may need to be decreased, or the administration stopped.

The use of contaminated haemofiltration solution may cause sepsis, shock and fatal conditions.

Precautions for use:

Hemosol B0 may be warmed to 37 °C to enhance patient comfort. Warming of the solution prior to use should be done before reconstitution with dry heat only. Solutions should not be heated in water or in a microwave oven. The solution should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not administer unless the solution is clear and the seal is intact.

Before and during treatment, electrolyte and acid-base balance should be closely monitored throughout the procedure. Phosphate up to 1.2 mmol/L may be added to the solution. If potassium phosphate is added, the total potassium concentration should not exceed 4 mEq/L (4 mmol/L). Potassium supplement might be necessary.

The patient's hemodynamic status and fluid balance should be monitored throughout the procedure and corrected as needed.

Paediatric population:

There are no specific warnings and precautions when using this medicine for children.

4.5 Interaction with other medicinal products and other forms of interaction

The blood concentration of filterable/dialysable drugs may be reduced during treatment. Corresponding corrective therapy should be instituted if necessary to establish the desired blood concentrations for drugs removed during treatment.
Interactions with other medications due to electrolyte and/or acid-base imbalances can be avoided by correct dosage of the solution for haemodialysis/haemofiltration and precise monitoring.
- However, the following interactions are conceivable:
- The risk of digitalis-induced cardiac arrhythmia is increased during hypokalaemia;
- Vitamin D and vitamin D analogues, as well as medicinal products containing calcium (e.g. calcium chloride or calcium gluconate used for maintenance of calcium homeostasis, in CRRT patients receiving citrate anticoagulation and calcium carbonate as phosphate binder) can increase the risk of hypercalcaemia;
- Additional sodium hydrogen carbonate (or other buffer source) contained in the CRRT fluids or in other fluids administered during therapymay increase the risk of metabolic alkalosis;
- When citrate is used as an anticoagulant, it contributes to the overall buffer load and can reduce plasma calcium levels.

4.6 Fertility, pregnancy and lactation

Pregnancy and breastfeeding
No effects during pregnancy or on the breast-fed newborn/infant are anticipated. There is no report on Hemosol B0 during pregnancy or lactation but literature on renal replacement therapy during acute kidney injury does not suggest risks associated with solutions. The prescriber should consider the benefit/risk relationship before administering Hemosol B0 to pregnant or breast feeding women.

Fertility
There are no clinical data on fertility. However no effects on fertility are anticipated.

4.7 Effects on ability to drive and use machines

Not relevant

4.8 Undesirable effects

The following undesirable effects are reported from post-marketing experience. The table presented below is according to the MedDRA system organ classification (SOC and Preferred Term Level).
Frequencies: Not known (cannot be estimated from the available data).

System Organ Class	Preferred Term	Frequency
Metabolism and nutrition disorders	Electrolyte imbalances, e.g.:hypophosphataemia, hypokalaemia	Not known
	Acid-base balance disorders	Not known
	Fluid imbalance	Not known
Vascular disorders	Hypotension	Not known
Gastrointestinal disorders	Nausea	Not known
	Vomiting	Not known
Musculoskeletal and connective tissue disorders	Muscle spasms	Not known

Special attention must be taken for patients with hypokalaemia as this solution is potassium-free (see section 4.4).

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation 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 via
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

4.9 Overdose

Overdose with Hemosol B0 substitution fluid should not occur if the procedure is carried out correctly and the fluid balance, electrolyte and acid-base balance of the patient are carefully monitored.
However, overdose could lead to severe consequences, such as congestive heart failure, electrolyte or acid-base disturbances. If hypervolaemia or hypovolaemia occur, this should be corrected immediately.
If electrolyte imbalance and acid-base balance abnormalities (e.g., metabolic alkalosis, hypophosphataemia, hypokalaemia, etc.) occur, stop administration promptly. There is no specific antidote for overdose. The risk can be minimized by close monitoring and adequate supplementation during treatment (see section 4.4).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Hemofiltrates, ATC code: B05ZB.

Pharmacodynamic effects
Hemosol B0 is pharmacologically inactive. The sodium, calcium, magnesium and chloride ions are present at concentrations similar to physiological levels in plasma.

Mechanism of action
The solution is used to replace water and electrolytes removed during haemofiltration or to serve as a suitable exchange medium for use during haemodiafiltration or continuous haemodialysis.Hydrogen carbonate is used as an alkalising buffer.

5.2 Pharmacokinetic properties

Not relevant. The active ingredients are pharmacologically inactive and are present at concentrations similar to physiological plasma levels.

5.3 Preclinical safety data

Not relevant. The active ingredients are pharmacologically inactive and are present at concentrations similar to physiological plasma levels.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

In the small compartment A: Water for injections

In the large compartment B: Water for injections, Carbon dioxide

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.
It is the responsibility of the physician to judge the incompatibility of an additive medication with the Hemosol B0 solution by checking for eventual colour change and/or eventual precipitation, insoluble complexes or crystals. The Instructions for Use of the medication to be added must be consulted.
Before adding a drug, verify it is soluble and stable in water at the pH of Hemosol B0 (pH of reconstituted solution is 7.0 to 8.5).
The compatible medication must be added to the reconstituted solution and the solution must be administered immediately.

6.3 Shelf life

18 months as packaged for sale.

Chemical and physical in-use stability of the reconstituted solution has been demonstrated for 24 hours at 22° C. From a microbiological point of view, once opened (i.e. connected to the line), and as hydrogen carbonate is present, the reconstituted solution should be used immediately. Other in-use storage times and conditions prior to use are the responsibility of the user and would not normally be longer than 24 hours, including the duration of the treatment.

6.4 Special precautions for storage

Do not store below +4°C.
For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

The container made in polyolefin is a two-compartment bag. The 5000 ml bag is comprised of a small compartment (250 ml) and a large compartment (4750 ml). The two compartments are separated by a peel seal.
The large compartment B is fitted with an injection connector (or spike connector) made of polycarbonate (PC)**,** which is closed with a rubber disc covered by a cap as well as a luer connector (PC) with a valve made of silicone rubber for the connection of the bag with a suitable replacement solution line or dialysis line.
The bag is over wrapped with a transparent overwrap made of multilayer polymer film.

Each two-compartment bag contains 5000 ml.
Package size: 2 x 5000 ml in a box.

6.6 Special precautions for disposal and other handling

The electrolyte solution (small compartment A) is added to the buffer solution (large compartment B) after opening the peel seal immediately before use to obtain the reconstituted solution.

A patient information leaflet with detailed instruction for use is enclosed in the box.
Aseptic technique should be used throughout the handling and administration to the patient:
Use only if the overwrap is not damaged, all seals are intact, frangible pin or peel seal is not broken, and the solution is clear.
Press bag firmly to test for any leakage. If leakage is discovered, discard the solution immediately since sterility can no longer be assured.

The large compartment is fitted with an injection port for the possible addition of other necessary drugs after reconstitution of the solution.
Before adding a substance or medication, verify that it is soluble and stable in Hemosol B0, and that the pH range is appropriate (pH of reconstituted solution is 7.0 to 8.5).

Additives may be incompatible. The instructions for use of the medication to be added and other relevant literature must be consulted. After addition, if there is a colour change and/or the appearance of precipitates, insoluble complexes, or crystals, do not use.

Mix the solution thoroughly when additives have been introduced. The introduction and mixing of additives must always be performed prior to connecting the solution bag to the extracorporeal circuit.

If a peel seal separates the two compartments of the bag and a valve is located in the luer connector the following instructions for use should be followed:
I Immediately before use remove the overwrap from the bag and mix the solutions in the two different compartments. Hold the small compartment with both hands and squeeze it until an opening is created in the peel seal between the two compartments.
II Push with both hands on the large compartment until the peel seal between the two compartments is entirely open.
III Secure complete mixing of the solution by shaking the bag gently. The solution is now ready for use, and can be hung on the equipment.
IV The dialysis or replacement line may be connected to either of the two access ports.
IVa If the luer access is used, remove the cap with a twist and pull motion, and connect the male luer lock on the dialysis or replacement line to the female luer receptor on the bag using a push and twist motion. Ensure that the connection is fully seated and tighten. The connector is now open. Verify that the fluid is flowing freely.
When the dialysis or replacement line is disconnected from the luer connector, the connector will close and the flow of the solution will stop. The luer port is a needle-less and swabbable port.
IVb If the injection port is used, first remove the snap-off cap. The injection port is a swabbable port. Then introduce the spike through the rubber septum. Verify that the fluid is flowing freely.

The solution should be used immediately after removal of the over wrap. If not used immediately, the reconstituted solution should be used within 24 hours, including the duration of the treatment, after addition of the electrolyte solution to the buffer solution.
The reconstituted solution is for single use only. Do not use if container is damaged or if solution is not clear. Discard any unused portion immediately after use.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Vantive Belgium SRL
Boulevard D'Angleterre 2
Braine-L'Alleud
1420
Belgium

8 MARKETING AUTHORISATION NUMBER

PA25288/005/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:11 June 1999

Date of last renewal: 15 October 2014

10 DATE OF REVISION OF THE TEXT

November 2024