Prismasol® 4

Bicarbonate-Buffered Solution for Continuous Hemodialysis, Hemofiltration and Hemodiafiltration

	mmol/l	mEq/l
Calcium Ca2+	1.75	3.50
Magnesium Mg2+	0.5	1.0
Sodium Na+	140	140
Chloride Cl-	113.5	113.5
Lactate-	3	3
Hydrogen carbonate HCO3-	32	32
Potassium K+	4	4
Glucose	6.1	

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Prismasol® 4 – Summary of product characteristics

1. Name of the medicinal product
Prismasol 4 mmol/l Potassium solution for hemofiltration and hemodialysis.

2. Qualitative and quantitative composition
Prismasol 4 mmol/l Potassium is presented in a two compartment bag containing in the smaller compartment A, the electrolyte solution, and in the larger compartment B, the buffer solution. The final reconstituted solution is obtained after breaking the frangible pin and mixing both solutions.

Before reconstitution
1000 ml of electrolyte solution (**small compartment A**) contains:

active substances:

Calcium chloride, 2 H_2O	5.145 g
Magnesium chloride, 6 H_2O	2.033 g
Glucose anhydrous (as glucose monohydrate)	22.00 g
(S)-Lactic acid (as lactic acid solution 90 % w/w)	5.400 g

1000 ml of buffer solution (**large compartment B**) contains:

active substances:

Sodium chloride	6.45 g
Potassium chloride	0.314 g
Sodium hydrogen carbonate	3.090 g

After reconstitution
1000 ml of the reconstituted solution contains:

	mmol/l	mEq/l
Calcium Ca^{2+}	1.75	3.50
Magnesium Mg^{2+}	0.5	1.0
Sodium Na^{+}	140	140
Chloride Cl^{-}	113.5	113.5
Lactate^{-}	3	3
Hydrogen carbonate HCO_3^{-}	32	32
Potassium K^{+}	4	4
Glucose	6.1	

Each liter of the final reconstituted solution corresponds to 50 ml of solution A and 950 ml of solution B.
For excipients, see 6.1

3. Pharmaceutical form
Solution for hemofiltration and hemodialysis.
Clear reconstituted solution with a slightly yellow color.
Theoretical Osmolarity: 301 mOsm/l
pH of the reconstituted solution: 7.0 - 8.5

4. Clinical particulars
4.1 Therapeutic Indications
Prismasol 4 mmol/l Potassium is used in the treatment of renal failure, as substitution solution in hemofiltration and hemodiafiltration and as dialysis solution in continuous hemodialysis or continuous hemodiafiltration.
Prismasol 4 mmol/l Potassium solution may also be used in case of drug poisoning with dialysable or filterable substances.
Prismasol 4 mmol/l Potassium solution is indicated in patients who are normokalaemic.

4.2 Posology and method of administration
Posology:
The volume of Prismasol 4 mmol/l Potassium used will depend on the clinical condition of the patient and the target fluid balance. The dose volume is therefore at the discretion of the responsible physician.
Flow rates for the substitution solution in hemofiltration and hemodiafiltration are:
Adult and adolescents: 500 - 3000 ml/hour
Children: 15 - 35 ml/kg/hour
Flow rates for the dialysis solution (dialysate) in continuous hemodialysis and continuous hemodiafiltration are:
Adult and adolescents: 500 - 2500 ml/hour
Children: 15 - 30 ml/kg/hour
Commonly used flow rates in adults are about 2000 ml/h which correspond to a daily amount of 55 l.
Method of administration:
Intravenous use and for hemodialysis.
Prismasol 4 mmol/l Potassium, when used as a substitution solution is administered into the circuit before (pre-dilution) or after the hemofilter (post-dilution). For further information on the use of the medicinal product see section 6.6 Instructions for use and handling.

4.3 Contra-indications
Solution dependent contra-indications
- Hyperkalemia
- Metabolic alkalosis

Hemofiltration/- dialysis dependent contra-indications
- Renal failure with pronounced hyper catabolism, if the uraemic symptoms cannot be corrected with hemofiltration
- Insufficient arterial pressure in the vascular access.
- Systemic anticoagulation (high risk of hemorrhage).

4.4 Special warnings and precautions for use
The solution should be used only by, or under the direction of, a physician competent in renal failure treatments using hemofiltration, hemodiafiltration and continuous hemodialysis.
Warnings:
Check that the solutions are clear and that all seals are intact before mixing. Carefully follow the instructions for use.
The electrolyte solution **must** be mixed with the buffer solution **before use** to obtain the reconstituted solution suitable for hemofiltration/ hemodiafiltration/continuous hemodialysis.
Do not administer the solution unless it is clear. Aseptic technique must be used during connection / disconnection of the line sets.
Use only with appropriate extra-renal replacement equipment.
Special precautions for use:
The heating of this solution to body temperature (37°C) must be carefully controlled verifying that the solution is clear and without particles.
Hemodynamic status, fluid balance, electrolyte and acid-base balance should be closely monitored throughout the procedure. Close monitoring of serum potassium levels must be carried out to enable the correct selection of the most appropriate potassium concentration.
The inorganic phosphate concentration should be measured regularly.
Inorganic phosphate must be substituted in cases of hypophosphatemia.
Blood glucose concentration should be closely monitored, especially in diabetic patients.
In case of fluid imbalance (example: cardiac failure, head trauma...), the clinical situation must be carefully monitored and balance must be restored.
The use of contaminated hemofiltration and hemodialysis solution may cause sepsis, shock and death.

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. Interactions with other medicaments can be avoided by correct dosage of the solution for hemofiltration and hemodialysis and precise monitoring.
However, the following interactions are conceivable:
- The risk of digitalis-induced cardiac arrhytmia is increased during hypokalemia;
- Vitamin D and medicinal products containing calcium, e.g. calcium carbonate as phosphate binder, can increase the risk of hypercalcaemia;
- Additional sodium bicarbonate substitution may increase the risk of metabolic alkalosis.

4.6 Pregnancy and lactation
There are no adequate data from the use of Prismasol 4 mmol/l Potassium in pregnant or lactating woman. The prescriber should consider the benefit/risk relationship before administering Prismasol 4 mmol/l Potassium to pregnant or breast-feeding women.

4.7 Effects on ability to drive and use machines
Not relevant

4.8 Undesirable effects
Undesirable effects can result from the solution used or the treatment.
Bicarbonate-buffered hemofiltration and hemodialysis solutions are generally well tolerated.
There have been no reports of adverse events or undesirable effects, that might possibly be associated with the bicarbonate-buffered solution for hemofiltration and hemodialysis.
However, the following undesirable effects are conceivable: Hyper- or hypo hydration, electrolyte disturbances, hypophosphatemia, hyper glycaemia and metabolic alkalosis.
Some undesirable effects related to the dialysis treatments (hemofiltration and hemodialysis) can occur, such as nausea, vomiting, muscle cramps and hypotension.

4.9 Overdose
Overdose with Prismasol 4 mmol/l Potassium, 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 will result in fluid overload in patients with renal failure.
Continued application of hemofiltration will remove excess fluid and electrolytes. In case of hyper hydration, the ultrafiltration must be increased and the rate of administration of the solution for hemofiltration reduced. In the case of a severe dehydration it is necessary to cease ultrafiltration and to increase the inflow of solution for hemofiltration appropriately.
Overdose could lead to severe consequences, such as congestive heart failure, electrolyte or acid-base disturbances.

5. Pharmacological properties
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Hemofiltrates. ATC code: B05ZB
Prismasol 4 mmol/l Potassium, solution for hemofiltration and hemodialysis is pharmacologically inactive. The sodium, calcium, magnesium, potassium, chloride ions and glucose are present at concentrations similar to physiological levels in plasma.
The solution is used to replace water and electrolytes removed during haemofiltration and hemodiafiltration or to serve as a suitable exchange medium for use during continuous hemodiafiltration or continuous hemodialysis. Hydrogen carbonate is used as an alkalizing 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
All the ingredients of the solution are physiological components in animal and human plasma.
Toxic effects are not expected at therapeutic doses.

6. Pharmaceutical particulars
6.1 List of excipients
Electrolyte solution (small compartment A): Water for injections
Buffer solution (large compartment B): Water for injections, Carbon dioxide

6.2 Incompatibilities
In the absence of compatibility studies, this 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 Prismasol 4 mmol/l Potassium solution by checking for eventual color 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 Prismasol 4 mmol/l Potassium (pH of reconstituted solutions 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
1 year 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 chemical point of view, the reconstituted solution should be used immediately. If not used immediately in-use storage times and conditions prior to use are the responsibility of the user and should 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.

6.5 Nature and contents of container
The container made in Poly(vinyl chloride) (PVC) is a two compartment bag. A frangible pin separates the two compartments. The large compartment B is fitted with an injection port for drug's admixture after reconstitution of the solution, as well as a luer connector for the connection of the bag with a suitable substitution fluid / dialysate line.
The bag is overwrapped with a transparent outer packaging made of multi layer copolymers.
The 5000 ml bag is composed of a small compartment (250 ml) and a large compartment bag (4750 ml).
Each two compartment bag contains 5000 ml.
Pack 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 breaking the frangible pin immediately before use.
A patient information leaflet with detailed instruction for use is enclosed in the box.
Aseptic technique should be used throughout administration to the patient:
Do not remove unit from overwrap until ready for use.
If a frangible pin separates the two compartments of the bag the following instructions should be followed:
I. Remove the overwrap from the bag and the sheet between the folded compartments.
Open the seal by breaking the frangible pin between the two compartments of the bag. The frangible pin will remain in the bag.
II. Make sure all the fluid from the small compartment A is transferred into the large compartment B.
III. Rinse the small compartment A **twice** by pressing the mixed solution back into the small compartment and then back into the large compartment B.
IV. When the small compartment A is empty: shake the large compartment B so that the contents mix completely. The solution is now ready for use.
V. If the luer connector is used, first connect the replacement or dialysate line and then break the frangible pin in the luer connector. The bag should hang in all three hanging holes when used.
Connect the substitution fluid/dialysate line. The reconstituted solution should be used immediately. 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 solution immediately after use.

7. Marketing authorization holder
Gambro Lundia AB - Box 10 101 - SE-220 10 Lund - SWEDEN.

8. Marketing authorization number
Zul. Nr.: 1-25100 Austria; 359 561-4 France; Zul. Nr.: 56625.01.00 Germany; MT.nr 34572 Denmark; MT.nr 17941 Finland; PA 785/6/2 Ireland; MT.nr 02-1624 Norway; MA 02-1624 Sweden; RVG 28877 The Netherlands; PL 14983/0014 United Kingdom; 6000 IE 35 F 12 Belgium; AUT 6000 EI 35 F12 Portugal; AIC 036146025/M Italy; 15129/03/11-2-2004 Greece.

9. Date of first authorization/Renewal of the authorization

10. Date of revision of the Text
27/07/2007

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