

PRESCRIBING INFORMATION

1. Name of the medicinal product

Prismasol 4 mmol/l Potassium solution for haemodialysis/haemofiltration

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 or peel seal and mixing both solutions.

BEFORE RECONSTITUTION

1 000 ml of electrolyte solution (small compartment A) contains:

active substances:

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

1 000 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

A+B

Calcium chloride, 2 H ₂ O	0.257 g
Magnesium chloride, 6 H ₂ O	0.102 g
Glucose anhydrous	1.100 g
Lactic acid	0.270 g
Sodium chloride	6.128 g
Potassium chloride	0.298 g
Sodium hydrogen carbonate	2.936 g

AFTER RECONSTITUTION

1 000 ml of the reconstituted solution contains:

Active substances		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 litre of the final reconstituted solution corresponds to 50 ml of electrolyte solution A and 950 ml of buffer solution B.

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Solution for haemodialysis/haemofiltration

Clear reconstituted solution with a slightly yellow colour.

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 haemofiltration and haemodiafiltration and as dialysis solution in continuous haemodialysis or continuous haemodiafiltration.

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 haemofiltration and haemodiafiltration are:

Adult and adolescents: 500 - 3000 ml/hour

Children: 15 - 35 ml/kg/hour

Flow rates for the dialysis solution (dialysate) in continuous haemodialysis and continuous haemodiafiltration 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:

With haemodialysis machines.

Prismasol 4 mmol/l Potassium, when used as a substitution solution is administered into the circuit before (pre-dilution) or after the haemofilter (post-dilution).

For further information on the use of the medicinal product see section 6.6 Special precautions for disposal and other handling

4.3 Contraindications

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

Solution dependent contraindications

- Hyperkalaemia
- Metabolic alkalosis.

Haemofiltration/- dialysis dependent contraindications

- Renal failure with pronounced hypercatabolism, if the uraemic symptoms cannot be corrected with haemofiltration,
- Insufficient arterial pressure in the vascular access,

- Systemic anticoagulation (high risk of haemorrhage).

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 haemofiltration, haemodiafiltration and continuous haemodialysis.

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 haemofiltration / haemodiafiltration / continuous haemodialysis.

Do not administer the solution unless it is clear. Aseptic technique must be used during connection / disconnection of the line sets.

Use only with an appropriate extra-renal replacement equipment.

Special precautions for use :

Heating of this solution to body temperature (+37°C) must be carefully controlled verifying that the solution is clear and without particles.

Haemodynamic 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 hypophosphataemia.

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 balancing must be restored.

The use of contaminated haemofiltration and haemodialysis 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 haemofiltration and haemodialysis and precise monitoring.

However, the following interactions are conceivable:

- The risk of digitalis-induced cardiac arrhythmia is increased during hypokalaemia;
- Vitamin D and medicinal products containing calcium, e.g. calcium carbonate as phosphate binder, can increase the risk of hypercalcaemia;
- Additional sodium hydrogen carbonate 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 woman.

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.

The following undesirable effects may occur:

System Organ Class	Undesirable effects
Metabolism and nutrition disorders	Fluid retention
	Dehydration
	Electrolyte imbalance
	Hypophosphataemia
	Hyperglycaemia
	Metabolic alkalosis
Vascular disorders	Hypotension*
Gastrointestinal disorders	Nausea*
	Vomiting*
Musculoskeletal and connective tissue disorders	Muscle spasms*

* undesirable effects related to the dialysis treatments (haemofiltration and haemodialysis)

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form

<http://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il>

4.9 Overdose

Overdose with Primasol 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 haemofiltration will remove excess fluid and electrolytes. In case of hyperhydration, the ultrafiltration must be increased and the rate of administration of the solution for haemofiltration reduced. In the case of a severe dehydration it is necessary to cease ultrafiltration and to increase the inflow of solution for haemofiltration 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

Primasol 4 mmol/l Potassium, solution for haemofiltration and haemodialysis 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 haemodiafiltration or to serve as a suitable exchange medium for use during continuous haemodiafiltration or continuous haemodialysis.

Hydrogen carbonate is used as an alkalisng 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 Priskasol 4 mmol/l Potassium 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 Priskasol 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

The expiry date of the product is indicated on the packaging materials.

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.

For storage conditions after reconstitution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

The container made in Poly(vinyl chloride) (PVC) or 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 frangible pin or 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 frangible pin (PC) or a valve made of silicone rubber for the connection of the bag with a suitable replacement solution line or dialysis line.

The bag is overwrapped with a transparent overwrap made of multilayer polymer film.

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 or opening the peel seal immediately before use.

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 and a frangible pin is located in the luer connector the following instructions for use 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 contents mix completely.

The solution is now ready for use.

V If the luer connector is used, first connect the replacement or dialysis 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/dialysis 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.

If a frangible pin separates the two compartments of the bag and a valve is located in the luer connector the following instructions for use shall be followed:

I Remove the over wrap from the bag immediately before use and discard any other packaging materials. 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 A 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 and the bag can be hung on the equipment.

V The dialysis or replacement line may be connected to either of the two access ports.

Va 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.

- Vb** If the injection port is used, first remove the snap-off cap. Then introduce the spike through the rubber septum. Verify that the fluid is flowing freely.

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.

If a peel seal separates the two compartments of the bag and a frangible pin 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 line may be connected to either of the two access ports.
- IVa** If the luer access is used, remove the cap and connect the male luer lock on the dialysis line to the female luer receptor on the bag; tighten. Using thumb and fingers, break the coloured frangible pin at its base, and move it back and forth. Do not use a tool. Verify that the pin is completely separated and that the fluid is flowing freely. The pin will remain in the luer port during the treatment.
- IVb** If the injection port is used, first remove the snap-off cap. Then introduce the spike through the rubber septum. Verify that the fluid is flowing freely.

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 portion.

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 shall be followed:

- I** Remove the overwrap from the bag immediately before use and discard any other packaging materials. Open the seal by holding the small compartment with both hands and squeezing 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. Then introduce the spike through the rubber septum. Verify that the fluid is flowing freely

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 portion.

7. Registration Number

152-98-34023-00

8. Manufacturer

Bieffe Medital S.P.A.,
Sondalo, Italy.

9. Licence Holder/Importer

Baxter Healthcare Distribution Ltd
34 Jerusalem St., Ra'anana, Israel.

This leaflet format has been determined by the Ministry of Health and the content has been checked and approved in November 2014.