

PRESCRIBING INFORMATION

PrismaSOL 4

Calcium chloride dihydrate 5.145 g/L, Glucose anhydrous 22.0 g/L, Lactic acid 5.4g/L, Magnesium chloride hexahydrate 2.033 g/L, Potassium chloride 0.314 g/L, Sodium bicarbonate 3.090 g/L, and Sodium chloride 6.45 g/L solution

Sterile solution for hemofiltration and hemodialysis

Hemodialytics, concentrates, ATC code: B05Z A

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PrismaSOL[®] 4

Calcium chloride dihydrate, Glucose anhydrous, Lactic acid solution 90% w/w, Magnesium chloride hexahydrate, Potassium chloride, Sodium bicarbonate, Sodium chloride

PART I: HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Route of Administration	Dosage Form / Strength	Clinically Relevant Nonmedicinal Ingredients
For intravenous infusion For hemodialysis	Sterile solution for hemofiltration and hemodialysis / Calcium chloride dihydrate 5.145 g/L, Glucose anhydrous 22.0 g/L, Lactic acid 5.4 g/L, Magnesium chloride hexahydrate 2.033 g/L, Potassium chloride 0.314 g/L, Sodium bicarbonate 3.09 g/L, and Sodium chloride 6.45 g/L solution.	Not relevant All non medicinal ingredients are pharmacologically inactive. For a complete listing see Dosage Forms, Composition and Packaging section of the prescribing information document.

INDICATIONS AND CLINICAL USE

PrismaSOL 4:

- Is used in the treatment of acute renal failure, as replacement solution in hemofiltration and hemodiafiltration and as dialysis solution in hemodialysis or hemodiafiltration in Continuous Renal Replacement Therapy (CRRT).
- Is indicated in patients who are normokalaemic.
- May also be used in case of drug poisoning with dialysable or filterable substances.

The solution should be used only by, or under the direction of, a physician competent in renal failure treatments using hemofiltration, hemodiafiltration and hemodialysis in CRRT.

Geriatrics (> 65 years of age):

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

Pediatrics (< 16 years of age):

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

CONTRAINDICATIONS

Solution dependent contraindications

- Hyperkalaemia
- Metabolic alkalosis

PrismaSOL 4 is contraindicated in patients with known hypersensitivity to the product

WARNINGS AND PRECAUTIONS**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 / hemodialysis in CRRT.

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

PrismaSOL 4 should be used with caution in patients with hyperkalemia. The serum potassium concentration must be monitored before and during hemofiltration and/or hemodialysis.

PrismaSOL 4 is a potassium-containing solution. If hyperkalemia occurs after treatment is initiated, additional sources of potassium influencing blood concentrations should be assessed. When PrismaSOL 4 is used as a replacement solution, decrease the infusion rate and confirm that the desired potassium concentration is achieved. If hyperkalemia does not resolve, stop the infusion promptly.

If hyperkalemia develops when PrismaSOL 4 is used as a dialysate, administration of a potassium-free dialysate may be necessary to increase the rate of potassium removal.

Solutions containing dextrose should be used with caution in patients with known allergy to corn or corn products. Because PrismaSOL 4 contains dextrose and lactate (which is metabolized to glucose), hyperglycemia may develop. Blood glucose levels should be monitored regularly. If hyperglycemia develops, administration of dextrose-free replacement

solution/dialysate may be necessary. Other corrective measures may be needed to maintain desired glycemic control.

The administration must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

PrismaSOL 4 contains hydrogen carbonate (bicarbonate), and lactate (a bicarbonate precursor) which can influence the patient's acid-base balance. If metabolic alkalosis develops during therapy with PrismaSOL 4, the administration should be stopped.

Special precautions for use:

The solution may be heated to no more than 37°C and this must be carefully controlled. After heating, verify that the solution remains clear and contains no particulate matter.

The use of contaminated hemofiltration and hemodialysis solution may cause sepsis and shock. The patient's hemodynamic status and fluid balance should be monitored throughout the procedure.

In case of hypervolemia, the net ultrafiltration rate prescribed for the CRRT device can be increased, and/or the rate of administration of solutions other than replacement fluid and/or dialysate can be reduced.

In case of hypovolemia, the net ultrafiltration rate prescribed for the CRRT device can be reduced, and/or the rate of administration of solutions other than replacement fluid and/or dialysate can be increased.

Special Populations

Pregnant Women: There are no adequate data from the use of PrismaSOL 4 in pregnant women. The prescribing physician should carefully consider the potential risks and benefits for each specific patient before administering this solution to pregnant women. PrismaSOL 4 may be considered during pregnancy if clearly needed.

Nursing Women: There are no adequate data from the use of PrismaSOL 4 in lactating women. The prescribing physician should carefully consider the potential risks and benefits for each specific patient before administering this solution to breast-feeding women.

Pediatrics (< 16 years of age): There are no special precautions for pediatric population.

Geriatrics (> 65 years of age): There are no special precautions for geriatric population.

Monitoring and Laboratory Tests

Hemodynamic status, fluid balance, electrolyte and acid-base balance should be closely monitored throughout the procedure.

Close monitoring of serum potassium concentrations 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.

ADVERSE REACTIONS

Adverse Drug Reaction Overview

Adverse drug reactions can result from the solution used or the treatment.

Bicarbonate-buffered hemofiltration and hemodialysis solutions are generally well tolerated. However, the following adverse drug reactions are conceivable:
Hyper- or hypohydration, electrolyte disturbances, hypophosphataemia, hyperglycaemia, metabolic alkalosis.

Some adverse reactions related to the dialysis treatments (hemofiltration and hemodialysis) can occur, such as nausea, vomiting and muscle cramps.

Other adverse reactions reported with similar products include

- Hypotension
- Acid–base balance disorders
- Electrolyte imbalance
- Fluid imbalance

Clinical Trial Adverse Drug Reactions

Not relevant, since this registration is based on published literature only.

Less Common Clinical Trial Adverse Drug Reactions (<1%)

Not relevant, since this registration is based on published literature only.

Abnormal Hematologic and Clinical Chemistry Findings

Not relevant, since this registration is based on published literature only.

Post-Market Adverse Drug Reactions

Similar solutions as PrismaSOL 4 are registered in some European countries, Asiatic countries and in USA.

INVESTIGATIONS: Calcium ionized increased

DRUG INTERACTIONS

Overview

The blood concentration of filterable/dialysable drugs may be reduced during treatment due to their removal by the extracorporeal filter. Corresponding corrective therapy should be instituted if necessary to establish the desired blood concentrations for drugs removed during treatment. Interactions with other medications can be avoided by correct dosage of the solution for hemofiltration and hemodialysis and precise monitoring.

It is the responsibility of the physician to consider the compatibility of any medication that is to be mixed with the PrismaSOL 4 solution, by checking for colour change and precipitation of insoluble complexes or crystals. The Instructions for Use of the medication to be added must be consulted.

The compatible medication must be added to the reconstituted solution and the solution must be administered immediately.

Medication should only be added under the direction of a physician in the following way: Remove any fluid from injection port, hold the bag upside down, insert the drug through the injection port and mix thoroughly. When introducing additives, use aseptic techniques. **The solution must be administered immediately.**

Drug-Drug Interactions

Interactions with other drugs have not been established.

However, the following interactions are conceivable:

- The risk of digitalis-induced cardiac arrhythmia is increased during hypokalaemia;
- Vitamin D and other 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) can increase the risk of hypercalcaemia;
- Additional sodium bicarbonate (or buffer source) contained in the CRRT fluids or in other fluids administered during therapy may 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.

Drug-Food Interactions

Interactions with food have not been established.

Drug-Herb Interactions

Interactions with herbal products have not been established.

Drug-Laboratory Interactions

Interactions with laboratory tests have not been established.

DOSAGE AND ADMINISTRATION

Dosing Considerations

The rate at which PrismaSOL 4 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 depend on 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.

Phosphate up to 1.2 mmol/L may be added to PrismaSOL 4. Use sodium phosphate if adding phosphate to the bag.

Recommended Dose and Dosage Adjustment

The approximate range of commonly used flow rates for the replacement solution in hemofiltration and hemodiafiltration are:

Adults:	500 - 3000 mL/h
Children (including adolescents to 18 years):	1000 - 4000 mL/h/1.73 m ²

The approximate range of commonly used flow rates for the dialysis solution (dialysate) in continuous hemodialysis and continuous hemodiafiltration are:

Adults:	500 - 2500 mL/hour
Children (including adolescents to 18 years):	1000 - 4000 mL/h/1.73 m ²

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. PrismaSOL 4 has an osmolarity of 301 mOsmol/L.

Missed Dose

Not relevant, since PrismaSOL 4 is administered continuously.

Administration

Intravenous use for hemofiltration (and part of hemodiafiltration) and dialysis transmembrane use for hemodialysis.

PrismaSOL 4 is used as a replacement solution and/or dialysate. PrismaSOL 4 when used as replacement solution, is administered into the extra-corporeal circuit before (pre-dilution) or after (post-dilution) the hemofilter or hemodiafilter

Use only with appropriate extracorporeal renal replacement equipment. PrismaSOL 4 may be warmed to 37 °C (98.6 °F) to enhance patient comfort. Warming of PrismaSOL 4 prior to use should be done before reconstitution with dry heat only (e.g., heating pad, warming plate). Solutions should not be heated in water or in a microwave oven due to the potential for patient injury or discomfort.

PrismaSOL 4 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.

Reconstitution:

The solution in the small compartment A is added to the solution in the large compartment B after breaking the frangible pin or peel seal immediately before use to obtain the reconstituted solution.

OVERDOSAGE

Overdose with PrismaSOL 4 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 can result in fluid overload in patients with renal failure. Electrolyte imbalance and acid-base balance abnormalities (e.g., metabolic alkalosis, Hypophosphatemia, Hypokalemia, etc.) may occur in the event of an overdose. Stop administration promptly. There is no specific antidote for overdose. The risk can be minimized by close monitoring during treatment.

Overdose could lead to severe consequences, such as congestive heart failure, electrolyte or acid-base disturbances.

For management of suspected overdose, please contact the regional poison centre.
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ACTION AND CLINICAL PHARMACOLOGY

Mechanism of Action

PrismaSOL 4 is pharmacologically inactive. The sodium, potassium, calcium, magnesium, 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 hemofiltration and hemodiafiltration or to serve as a suitable exchange medium for use during hemodiafiltration or hemodialysis in CRRT.

Bicarbonate is used as an alkalising buffer.

Glucose is intended to help normalise glucose balance.

Pharmacodynamics

No factor affects the pharmacodynamic response.

Pharmacokinetics

Not relevant, since the drug substances are pharmacologically inactive and are present at concentrations similar to physiological plasma levels.

Special Populations and Conditions

Not relevant, since the pharmacokinetics are not modified with specific population and conditions.

STORAGE AND STABILITY

Store between +4°C and +30°C. Do not refrigerate. Protect from freezing.

Chemical and physical in-use stability of the reconstituted solutions has been demonstrated for 24 hours at 22° C. 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.

Do not use if container is damaged or if solution is not clear.

SPECIAL HANDLING INSTRUCTIONS

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.

Do not remove unit from over wrap until ready for use.

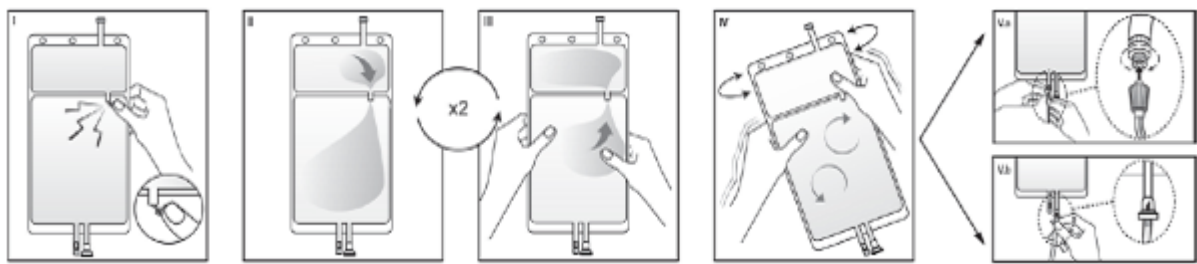
The reconstituted solution should be used immediately (not to exceed 24 hours)

The reconstituted solution is for single use only.

Discard any unused portion.

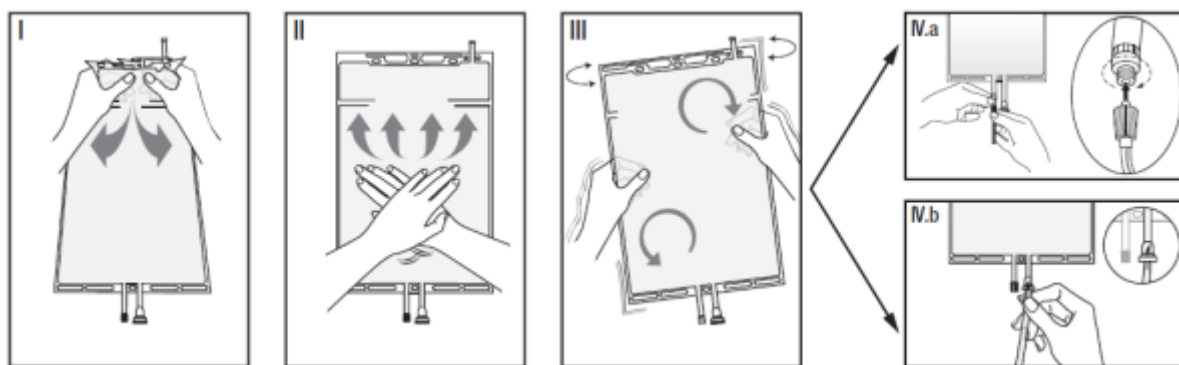
If a frangible pin separates the two compartments of the bag the following instructions for use should be followed:

- I** Remove the over wrap from the bag and the sheet between the folded compartments immediately before use. 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 and can be hung on the equipment. The bag should hang in all three hanging holes when used. The dialysis or replacement line may be connected to the luer access or the injection port.
- Va** If the luer access is used, using aseptic technique, 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 and tighten. The connector is now open. Verify that the fluid is flowing freely. (See figure Va below). 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. (See figure Vb below).



If a peel seal separates the two compartments of the bag the following instructions for use should be followed:

- I** Remove the over wrap from the bag immediately before use and discard any other packaging materials. Open the seal by holding the small compartment with both hands and squeeze it until an opening is created in the peel seal between the two compartments. (See figure I below)
- II** Push with both hands on the large compartment until the peel seal between the two compartments is entirely open. (See figure II below)
- 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. (See figure III below)
- IV** The dialysis or replacement line may be connected to the luer access or the injection port.
IVa If the luer access is used, using aseptic technique, 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. (See figure IV.a below). 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. (See figure IV.b below)



Adding a substance or medication to the solution:

Before adding a substance or medication, verify that it is soluble and stable in PrismaSOL 4, and that the pH range of PrismaSOL 4 is appropriate (pH of reconstituted solution is 7.0 to 8.5).

Mix the solution thoroughly when additives have been introduced

The large compartment is fitted with an injection port for the possible addition of other necessary drugs after reconstitution of the solution. 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 color change and/or the appearance of precipitates, insoluble complexes, or crystals, do not use.

DOSAGE FORMS, COMPOSITION AND PACKAGING

The container made in Poly(vinyl chloride) (PVC) or polyolefin (polypropylene based, multilayer laminates) materials is a two-compartment bag. A peel seal or 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 replacement fluid / dialysate line.

The bag is overwrapped with a transparent outer packaging made of multilayer copolymers.

The 5000 mL bag is composed of a small compartment (250 mL) and a large compartment bag (4750 mL). The solutions are sterile.

Each two compartment bag contains 5000 mL.

Pack size: 2 x 5000 mL in a box

Composition of PrismaSOL 4 before reconstitution

BEFORE RECONSTITUTION	PrismaSOL 4
Small compartment A (250 mL)	
Calcium chloride, dihydrate	5.145 g/L
Magnesium chloride, hexahydrate	2.033 g/L
Glucose anhydrous	22.000 g/L
(as glucose monohydrate)	24.200 g/L)
(S) Lactic acid	5.400 g/L
(as lactic acid solution 90 % w/w)	6.000 g/L)
Water for injections	to 1000 mL
Large compartment B (4750 mL)	
Sodium chloride	6.450 g/L
Sodium bicarbonate	3.090 g/L
Potassium chloride	0.314 g/L
Water for injections	to 1000 mL
Carbon dioxide	pH adjuster

Composition of PrismaSOL 4 after reconstitution

AFTER RECONSTITUTION		PrismaSOL 4	
		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		3.0	3.0
Bicarbonate	HCO ₃ ⁻	32	32
Potassium	K ⁺	4.0	4.0
Glucose		6.1	

Theoretical osmolarity: 301 mOsm/L

PART II: SCIENTIFIC INFORMATION

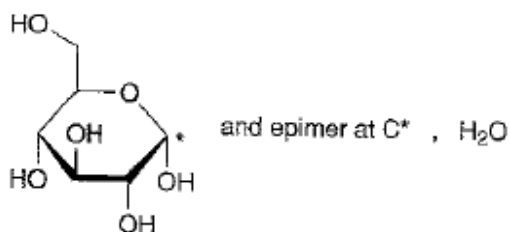
PHARMACEUTICAL INFORMATION

Drug Substance 1

Proper name: Glucose Monohydrate
Chemical name: Glucose Monohydrate

Molecular formula and molecular mass:
 $C_6H_{12}O_6 \cdot H_2O$.
 M_r : 198.2 g/mol

Structural formula:



Physicochemical properties:

Appearance: Glucose Monohydrate is a white crystalline powder with a sweet taste.

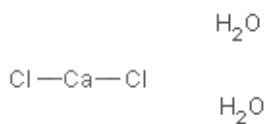
Solubility: Glucose Monohydrate is freely soluble in water, and sparingly soluble in alcohol.

Drug Substance 2

Proper name: Calcium Chloride Dihydrate
Chemical name: Calcium Chloride Dihydrate

Molecular formula and molecular mass:
 $CaCl_2 \cdot 2H_2O$.
 M_r : 147.0 g/mol

Structural formula:



Physicochemical properties:

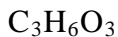
Appearance: Calcium Chloride Dihydrate is a white crystalline powder.

Solubility: Calcium Chloride Dihydrate is freely soluble in water, and soluble in alcohol.

Drug Substance 3

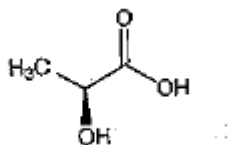
Proper name: Lactic Acid Solution 90% w/w
Chemical name: Lactic Acid Solution 90% w/w

Molecular formula and molecular mass:



M_r : 90.078 g/mol

Structural formula:



Physicochemical properties:

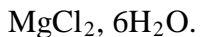
Appearance: Lactic Acid Solution 90% w/w is colourless or slightly yellow, syrupy liquid.

Solubility: Miscible with water and with ethanol (96 per cent).

Drug Substance 4

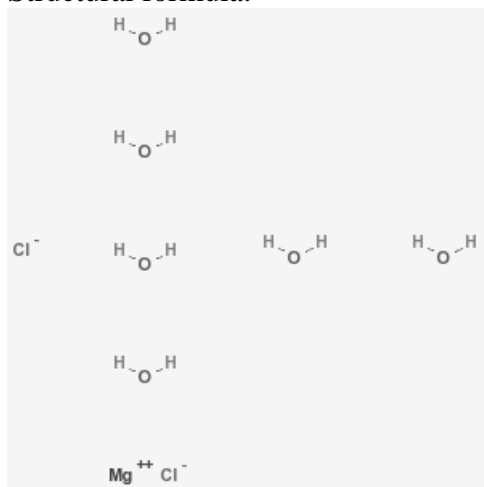
Proper name: Magnesium Chloride Hexahydrate
Chemical name: Magnesium Chloride Hexahydrate

Molecular formula and molecular mass:



M_r : 203.3 g/mol

Structural formula:



Physicochemical properties:

Appearance: Magnesium Chloride Hexahydrate is a colourless crystal.

Solubility: Magnesium Chloride Hexahydrate is freely soluble in water, freely soluble in alcohol.

Drug Substance 5

Proper name: Potassium Chloride
Chemical name: Potassium Chloride

Molecular formula and molecular mass:

KCl.

M_r : 74.6 g/mol

Structural formula:



Physicochemical properties:

Appearance: Potassium Chloride is a white or almost white crystalline powder or colourless crystals.

Solubility: Potassium Chloride is freely soluble in water, and practically insoluble in anhydrous ethanol.

Drug Substance 6

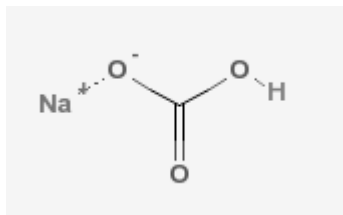
Proper name: Sodium Bicarbonate
Chemical name: Sodium Bicarbonate

Molecular formula and molecular mass:

NaHCO₃.

M_r : 84.0 g/mol

Structural formula:



Physicochemical properties:

Appearance: Sodium Bicarbonate is a white crystalline powder.

Solubility: Sodium Bicarbonate is soluble in water, practically insoluble in alcohol.

Other Properties: When heated in the dry state or in solution it gradually changes into sodium carbonate.

Drug Substance 7

Proper name: Sodium Chloride
Chemical name: Sodium Chloride

Molecular formula and molecular mass:

NaCl.

M_r : 58.44 g/mol

Structural formula:



Physicochemical properties:

Appearance: Sodium Chloride is a white crystalline powder or is presented as colourless crystals or white pearls.

Solubility: Sodium Chloride is freely soluble in water, and practically insoluble in ethanol.

CLINICAL TRIALS

Since PrismaSOL 4 is based on concentrations of electrolytes and glucose already in use in the treatment of Acute Renal Failure (ARF) in Continuous Renal Replacement Therapy (CRRT), application has therefore been supported by a review of published literature. There was no specific clinical trial initiated by the applicant for the development of the formulations of this solution.

CRRT replacement solutions for hemofiltration and hemodiafiltration and dialysis solution for hemodialysis and hemodiafiltration with formulations similar to PrismaSOL 4 have been in use worldwide for many years. There is extensive clinical experience provided in the scientific literature which has demonstrated these solutions to be both safe and effective when used as replacement and dialysis solutions for CRRT.

DETAILED PHARMACOLOGY

Pharmacological studies with PrismaSOL 4 have not been performed. The omission of preclinical studies is justified by the clinical experience with solutions with similar composition as PrismaSOL 4, used for hemofiltration and hemodialysis. Furthermore, the composition of the reconstituted solution complies with the Ph. Eur. monographs on solutions for hemofiltration / hemodiafiltration and hemodialysis.

MICROBIOLOGY

Not applicable

TOXICOLOGY

Toxicological studies with PrismaSOL 4 have not been performed. The omission of preclinical studies is justified by the clinical experience with solutions with similar composition as PrismaSOL 4, used for hemofiltration and hemodialysis. Furthermore, the composition of the reconstituted solution complies with the Ph. Eur. monographs on solutions for hemofiltration / hemodiafiltration and hemodialysis.

PART III: CONSUMER INFORMATION

PrismaSOL[®] 4

(Calcium chloride dihydrate, Glucose anhydrous, Lactic acid solution 90% w/w, Magnesium chloride hexahydrate, Potassium chloride, Sodium bicarbonate, Sodium chloride)

PLEASE READ ALL OF THIS CONSUMER INFORMATION CAREFULLY BEFORE YOU ARE ADMINISTERED THIS MEDICINE.

This leaflet is designed for consumers and is derived from the prescribing information document for this product, published when PrismaSOL 4 was approved for sale in Canada. This leaflet is a summary and will not tell you everything about PrismaSOL 4. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

PrismaSOL 4

- Is used by your doctor (or healthcare professional) in the treatment of acute kidney disease as solution for hemofiltration or hemodiafiltration (as replacement for fluid lost from the blood passing through a filter) and hemodialysis or hemodiafiltration (the blood flows on one side of a dialysis membrane while a hemodialysis solution flows on the other side of the membrane) in Continuous Renal Replacement Therapy (CRRT).
- Is indicated particularly in patients who are normokalaemic (anormal potassium concentration in your blood).
- May also be used in case of drug poisoning with dialysable or filterable substances.

What it does:

PrismaSOL 4 is a solution for hemofiltration, hemodiafiltration and hemodialysis in Continuous Renal Replacement Therapy. These techniques aim at normalising the composition of the blood.

When it should not be used:

PrismaSOL 4 should not be used in the following cases:

- Hyperkalaemia (a high concentration of potassium in your blood)
- Metabolic alkalosis (a process that primarily raises the plasma bicarbonate concentration)
- Hypersensitivity to PrismaSOL 4

Hemofiltration/ dialysis should not be used in the following cases:

- Kidney failure with pronounced hypercatabolism (abnormally increased destructive breakdown of complex substances in the body), if the uraemic symptoms (symptoms caused by high concentration of urea in your blood) cannot be corrected with hemofiltration,
- Insufficient arterial (blood) pressure in the vascular access (catheter area),

- Systemic anticoagulation (reduced clotting of your blood), if there is a high risk of hemorrhage (bleeding).

What the medicinal ingredients are:

Calcium chloride dihydrate, Glucose anhydrous, Lactic acid solution 90% w/w, Magnesium chloride hexahydrate, Potassium chloride, Sodium bicarbonate, Sodium chloride.

What the important nonmedicinal ingredients are:

Carbon dioxide
Water for Injections

What dosage forms it comes in:

Solution for hemofiltration and for hemodialysis.

WARNINGS AND PRECAUTIONS

The solution should be used only by, or under the direction of, a physician competent in renal failure treatments using hemofiltration, hemodiafiltration and hemodialysis.

Before and during treatment, your blood condition will be checked, e.g. your acid-base balance and concentrations of salts in the blood (electrolytes).

Your blood glucose concentration should be closely monitored, especially if you are diabetic.

Solutions containing dextrose should be used with caution in patients with known allergy to corn or corn products.

Tell your doctor if you are pregnant, planning to become pregnant or nursing.

The product will be checked to ensure that all seals are intact and the reconstituted solution is clear and free of precipitate.

INTERACTIONS WITH THIS MEDICATION

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

The blood concentration of some of your other medicines may be reduced during the treatment. Your doctor will decide if your medication should be changed.

In particular tell your doctor if you are taking:

- Digitalis. The risk of digitalis (medicine for treatment of certain heart conditions)-induced cardiac arrhythmia (irregular or rapid beating of the heart) is increased during hypokalaemia (low concentration of potassium in your blood).
- Vitamin D and other 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) can increase the risk of hypercalcaemia (a high concentration of calcium in your blood).

- Additional sodium bicarbonate [or buffer source] contained in the CRRT fluids or in other fluids administered during therapy may increase the risk of metabolic alkalosis (a process that primarily raises the plasma bicarbonate concentration).
- When citrate is used as an anticoagulant, it contributes to the overall buffer load and can reduce plasma calcium levels.

PROPER USE OF THIS MEDICATION

Usual dose:

PrismaSOL 4 is used as a replacement solution and/or dialysate.

The rate at which PrismaSOL 4 is administered depends on the blood concentration of electrolytes, acid-base balance, fluid balance and overall clinical condition of the patient. The volume of PrismaSOL 4 replacement solution and/or dialysate to be administered will depend on 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.

The approximate range of flow rates for the replacement solution in hemofiltration and hemodiafiltration are:

Adults:	500 - 3000 mL/h
Children:	1000 - 4000 mL/h/1.73m ² (including adolescents to 18 years)

The approximate range of flow rates for the dialysate solution in continuous hemodialysis and continuous hemodiafiltration are:

Adults:	500 - 2500 mL/h
Children:	1000 - 4000 mL/h/1.73m ² (including adolescents to 18 years)

Overdose:

Your fluid balance, electrolyte and acid-base balance will be carefully monitored.

Overdose could lead to severe consequences, such as congestive heart failure, electrolyte or acid-base disturbances.

If you have any further questions on the use of this product, please ask your doctor or pharmacist.

Missed Dose:

Not applicable as continuous treatment.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, PrismaSOL 4 can cause side effects, although not everybody gets them.

The following undesirable effects related to the solution are conceivable: Hyper- or hypohydration (abnormally high or low

volume of water in your body), electrolyte imbalance (salt in your blood) disturbances, hypophosphataemia (abnormally low concentration of phosphate in your blood), hyperglycaemia (abnormally high concentration of glucose in your blood) and metabolic alkalosis (a process that primarily raises the plasma bicarbonate concentration).

Some undesirable effects related to the dialysis treatments can occur, such as nausea, vomiting, muscle cramps and hypotension (low blood pressure).

Other adverse reactions reported with similar products include hypotension, acid-base balance disorders, electrolyte imbalance, fluid imbalance and increased ionized calcium.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

HOW TO STORE IT

Keep out of the reach of children

Store between +4°C and +30°C. Do not refrigerate. Protect from freezing

Chemical and physical in-use stability of the reconstituted solution has been demonstrated for 24 hours at 22° C.

The solution may be heated to no more than +37°C to enhance patient comfort. Warming of PrismaSOL 4 prior to use should be done before reconstitution with dry heat only (e.g., heating pad, warming plate). Solutions should not be heated in water or in a microwave oven due to the potential for patient injury or discomfort. After heating, verify that the solution is clear and without particles. Use immediately after mixing, or before the in-use storage directions above have expired, then discards the remaining solution. Storage conditions prior to use are the responsibility of the user.

Do not use after the expired date printed on the label and the packaging.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
Health Canada
Postal Locator 0701E
Ottawa, ON K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document, plus the full prescribing information, prepared for health professionals can be found at: by contacting the sponsor, Baxter Corporation, at: 1-800-387-8399

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