HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use PRISMASOL and PHOXILLUM safely and effectively.
See full prescribing information for PRISMASOL and PHOXILLUM.

PRISMASOL renal replacement solution
PRISMASOL Initial U.S. Approval: 2006

PHOXILLUM renal replacement solution
PHOXILLUM Initial U.S Approval: 2015

----------RECENT MAJOR CHANGES----------

Dosage and Administration	12/2015
Warnings and Precautions	01/2015

----------INDICATIONS AND USAGE----------

PRISMASOL and PHOXILLUM solutions are indicated:

- As a replacement solution in Continuous Renal Replacement Therapy (CRRT) and in case of drug poisoning when CRRT is used to remove dialyzable substances (1)

----------DOSAGE AND ADMINISTRATION----------

- Therapy must be individualized based on the patient's clinical condition, fluid, electrolyte, acid-base and glucose balance (2.1)
- Solution must be mixed prior to use (2.2)
- Use only with extracorporeal dialysis equipment appropriate for CRRT (2.3)

----------DOSAGE FORMS AND STRENGTHS----------

PRISMASOL and PHOXILLUM are available in multiple combinations of ingredients and in multiple variations of strengths. See full Prescribing Information for detailed descriptions of each formulation. (2, 3, 11)

----------CONTRAINDICATIONS----------

None (4)

---------- WARNINGS AND PRECAUTIONS----------

- Hemodynamic status and fluid, electrolyte and acid-base balance should be monitored. Abnormalities may be corrected by the use of appropriate formulations of PRISMASOL and PHOXILLUM solutions (5.1)
- Antidiabetic therapy may need adjustment during treatment with dextrose containing formulations (5.2)

To report SUSPECTED ADVERSE REACTIONS, contact Baxter at 1-866-888-2472 or FDA 1-800-FDA-1088 or www.fda.gov/medwatch

Revised: 12/2015

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

PRISMASOL and PHOXILLUM solutions are indicated in pediatric and adult patients for use as a replacement solution in Continuous Renal Replacement Therapy (CRRT) to replace plasma volume removed by ultrafiltration and to correct electrolyte and acid-base imbalances.They may also be used in case of drug poisoning when CRRT is used to remove dialyzable substances.

2 DOSAGE AND ADMINISTRATION

2.1 Administration Instructions

Visually inspect PRISMASOL and PHOXILLUM for particulate matter and discoloration prior to administration.

Administration should only be under the direction of a physician competent in intensive care treatment including CRRT. Use only with extracorporeal dialysis equipment appropriate for CRRT.

The prepared solution is for single patient use only.

Aseptic technique should be used throughout administration to the patient.

Discard any unused solution.

2.2 Dosing Considerations

PRISMASOL replacement solutions contain 4 different combinations of active ingredients (8 different products with varying ingredient amounts). PHOXILLUM replacement solutions contain 2 different combinations of active ingredients (2 different products with varying ingredient amounts). PRISMASOL and PHOXILLUM are supplied in a two-compartment bag that must be mixed immediately prior to use *[see Dosage and Administration (2.3)]:*

- Small compartment A (250 mL) containing an electrolyte solution, and
- Large compartment B (4750 mL) containing the buffer solution.

See Table 1 for the concentrations of the active ingredients (after mixing) in these 10 different replacement solutions (total volume is 5 Liters).

Table 1: Concentrations of Active Ingredients in the 8 PRISMASOL and 2 PHOXILLUM Replacement Solutions after Mixing

	Ca^{2+} mEq/L	HCO_3^- mEq/L	K^+ mEq/L	Mg^{2+} mEq/L	Na^+ mEq/L	HPO_4^{2-} mmol/L	Cl^- mEq/L	Lactate mEq/L	Dextrose mg/dL	Osmolarity mOsm/L
PRISMASOL Replacement Solutions										
BGK0/2.5	2.5	32	0	1.5	140	0	109	3	100	292
BGK4/2.5	2.5	32	4	1.5	140	0	113	3	100	300
BGK4/3.5	3.5	32	4	1	140	0	113.5	3	100	300
BGK2/3.5	3.5	32	2	1	140	0	111.5	3	100	296
BGK2/0	0	32	2	1	140	0	108	3	100	291
B22GK4/0	0	22	4	1.5	140	0	120.5	3	100	296
BGK4/0/1.2	0	32	4	1.2	140	0	110.2	3	100	295
BK0/0/1.2	0	32	0	1.2	140	0	106.2	3	0	282

PHOXILLUM Replacement Solutions										
BK4/2.5	2.5	32	4	1.5	140	1	114.5	0	0	294
B22K4/0	0	22	4	1.5	140	1	122	0	0	290

Ca^{2+} = calcium, HCO_3^- = bicarbonate, K^+ = potassium, Mg^{2+} = magnesium, Na^+ = sodium, HPO_4^{2-} = phosphate, Cl- = chloride; osmolarity is estimated

Select the mode of therapy, solute formulation, flow rates, and length of PRISMASOL and PHOXILLIUM replacement therapy in CRRT based on the patient's clinical condition, and fluid, electrolyte, acid-base, glucose balance. Administer either PRISMASOL or PHOXILLUM into the extracorporeal circuit:

- Before (pre-dilution) the hemofilter or hemodiafilter,
- After (post-dilution) the hemofilter or hemodiafilter, or
- Before and after the hemofilter or hemodiafilter.

2.3 Preparing the Solution

Use only if the overwrap is not damaged, all seals are intact, and the solution is clear. Press bag firmly to test for any leakage. Do not use if container is damaged or leaking.

The solution may be heated to no more than 40°C/104°F inside of the overwrap. After heating, verify that the solution remains clear and contains no particulate matter.

The solutions are supplied in two different two-compartment bags, one made of polyvinyl chloride with a frangible pin separating compartment A and B (see Figure 1) and one made of polyolefin with a peel seal separating compartment A and B (see Figure 6).

Follow the instructions below when connecting the solution bags for correct use of the access ports.

Instructions for preparing solutions supplied in a two-compartment, polyvinyl chloride (PVC) bag with a red frangible pin:

Figure 1

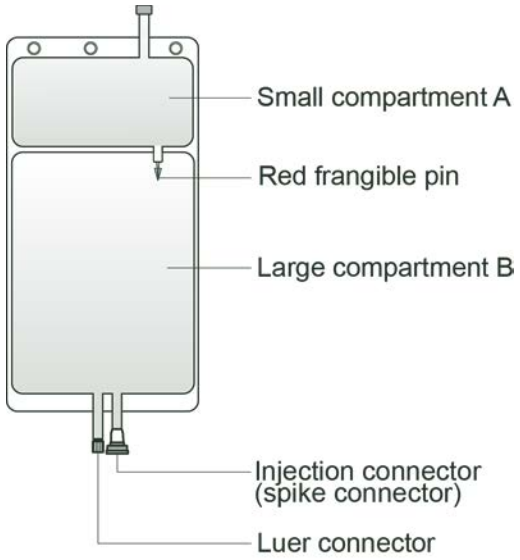


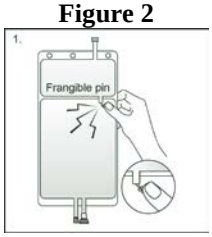
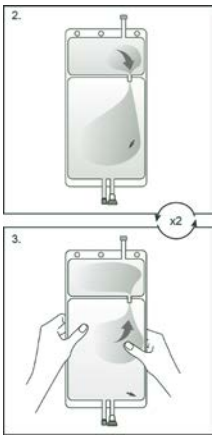
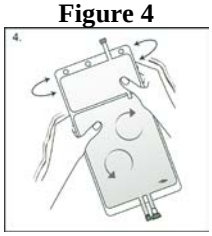
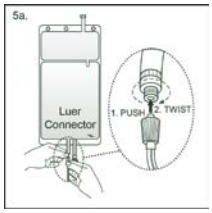
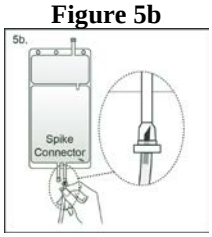
Figure 2 	**Step 1** Immediately before use, remove the overwrap from the bag and mix the solutions in the two different compartments. As soon as the overwrap is removed, the reconstitution of compartments A and B should be done and the mixed solution should be used immediately. After removal of the overwrap, the solution is stable for 24 hours including the duration of the treatment. Open the seal by breaking the red frangible pin between the two compartments of the bag. The frangible pin will remain in the bag. (See Figure 2 beside)
Figure 3 	**Step 2** Make sure all the fluid from the small compartment A is transferred into the large compartment B. (See Figure 3 beside)
	Step 3 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. (See Figure 3 beside)
Figure 4 	**Step 4** When the small compartment A is empty, shake the large compartment B so that the contents mix completely. (See Figure 4 beside) The solution is now ready to use and the bag can be hung on the equipment.
Figure 5a 	**Step 5** The replacement line may be connected to the bag through either the luer connector or the injection connector (spike connector). **Step 5a** The luer connector is a needle-less and swabbable connector. Remove the cap with a twist and pull motion, and connect the male luer lock on the replacement line to the female luer receptor on the bag. (See Figure 5a beside) Ensure that the connection is fully seated and tighten. The connector is now open. Verify that the fluid is flowing freely during use. When the replacement line is disconnected from the luer connector, the connector will close and the flow of the solution will stop.

Figure 5b	
	**Step 5b** If the injection connector (spike connector) is used, first remove the snap-off cap. Then introduce the replacement line spike through the rubber septum of the bag connector. (See Figure 5b beside) Ensure that the spike is fully inserted and verify that the fluid is flowing freely during use.

Instructions for preparing solutions supplied in a two-compartment, polyolefin bag with a peel seal:

Figure 6

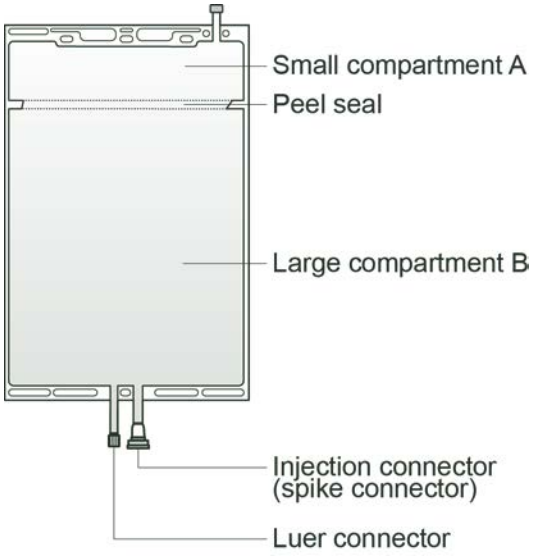


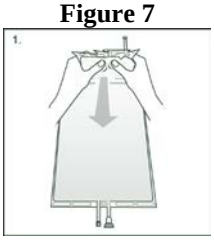
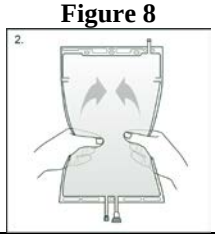
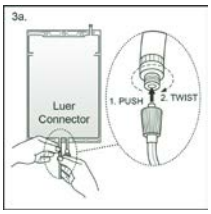
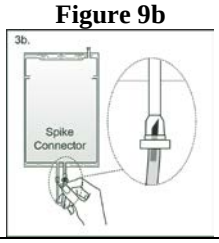
Figure 7	
	**Step 1** Immediately before use, remove the overwrap from the bag and mix the solutions in the two different compartments. As soon as the overwrap is removed, the reconstitution of compartments A and B should be done and the mixed solution should be used immediately. After removal of the overwrap, the solution is stable for 24 hours including the duration of the treatment. Hold the small compartment with both hands and squeeze it until an opening is created in the peel seal. (See Figure 7 beside)
Figure 8	
	**Step 2** Squeeze with both hands on the large compartment until the peel seal between the two compartments is entirely open. Shake gently to mix. (See Figure 8 beside) The solution is now ready to use and the bag can be hung on the equipment.

Figure 9a  	**Step 3** The replacement line may be connected to the bag through either of the luer connector or the injection connector (spike connector). **Step 3a** The luer connector is a needle-less and swabbable connector. Remove the cap with a twist and pull motion, and connect the male luer lock on the replacement line to the female luer receptor on the bag. (See Figure 9a beside) Ensure that the connection is fully seated and tighten. The connector is now open. Verify that the fluid is flowing freely during use. When the replacement line is disconnected from the luer connector, the connector will close and the flow of the solution will stop.
Figure 9b  	**Step 3b** If the injection connector (spike connector) is used, first remove the snap-off cap. Then introduce the replacement line spike through the rubber septum of the bag connector. (See Figure 9b beside) Ensure that the spike is fully inserted and verify that the fluid is flowing freely during use.

2.4 Adding Drugs to the Solutions

After mixing, additional drugs may be added to the bag via injection connector (spike connector) in large compartment B. In general, drugs other than phosphate should be administered through a different access line. When introducing additives, use aseptic techniques.

PRISMASOL Solutions:

Phosphate: 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.

PHOXILLUM Solutions:

Phosphate: Phosphate up to 0.2 mmol/L may be added to the solution. Use sodium phosphate if adding phosphate to bag. The total phosphate concentration should not exceed 1.2 mmol/L.

3 DOSAGE FORMS AND STRENGTHS

See Table 1 for the concentrations of the active ingredients (after mixing) in these 10 different replacement solutions *[see Dosage and Administration (2.2)]*.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Electrolyte and Volume Abnormalities

Monitor hemodynamic status and fluid, electrolyte and acid-base balance throughout the procedure. During hemofiltration or hemodiafiltration using PRISMASOL or PHOXILLUM replacement solutions, abnormalities in the plasma concentration of potassium, calcium, magnesium, and phosphate may develop. These abnormalities may be corrected by changing the formulations of replacement solution or by supplementation *[see Dosage and Administration (2)]*.

5.2 Hyperglycemia with Dextrose Containing Solutions

The use of PRISMASOL replacement solutions containing dextrose may increase the risk for hyperglycemia in patients with impaired glucose tolerance. Patients may require initiation of or modification of antidiabetic therapy during treatment with PRISMASOL solutions containing dextrose. Monitor blood glucose.

7 DRUG INTERACTIONS

As with the use of other replacement solutions, blood concentrations of dialyzable drugs may be influenced by CRRT. The blood concentrations of certain drugs may need to be monitored and appropriate therapy implemented to correct for removal during treatment.

7.1 Citrate

When used as an anticoagulant, citrate contributes to the overall buffer load and can reduce plasma calcium levels. Select the PRISMASOL/PHOXILLUM formulation(s) accordingly.

8 USE IN SPECIFIC POPULATION

8.1 Pregnancy

Pregnancy Category C

Animal reproduction studies have not been conducted with PRISMASOL and PHOXILLUM solutions. While there are no adequate and well controlled studies in pregnant women, appropriate administration of PRISMASOL and PHOXILLUM solutions with monitoring of fluid, electrolyte, acid-base and glucose balance, is not expected to cause fetal harm, or affect reproductive capacity. Maintenance of normal acid-base balance is important for fetal well-being.

8.3 Nursing Mothers

The components of PRISMASOL and PHOXILLUM solutions are excreted in human milk. Appropriate administration of PRISMASOL and PHOXILLUM solutions with monitoring of fluid, electrolyte, acid-base and glucose balance, is not expected to harm a nursing infant.

8.4 Pediatric Use

Safety and effectiveness have been established based on published clinical data of CRRT replacement solutions with compositions similar to PRISMASOL and PHOXILLUM used in adults and two hemofiltration studies in pediatric patients, including a study of newborns to 17 years old.

8.5 Geriatric Use

The experience with PRISMASOL and PHOXILLUM solutions in geriatric patients has not identified novel concerns.

11 DESCRIPTION

PRISMASOL and PHOXILLUM solutions are clear, sterile, free of bacterial endotoxins and contain no bacteriostatic or antimicrobial agents. These solutions are used in Continuous Renal Replacement Therapies (CRRT) as a replacement solution in hemofiltration and hemodiafiltration. Depending on the product (see Table 2), the two compartments contain:

Calcium chloride, USP, is chemically designated calcium chloride dihydrate ($CaCl_2 \cdot 2H_2O$).
Magnesium chloride, USP, is chemically designated magnesium chloride hexahydrate ($MgCl_2 \cdot 6H_2O$).
Sodium chloride, USP, is chemically designated NaCl.
Potassium chloride, USP, is chemically designated KCl.
Sodium bicarbonate, USP, is chemically designated $NaHCO_3$.
Dextrose, USP, is chemically designated D-Glucose anhydrous ($C_6H_{12}O_6$) or D-Glucose monohydrate ($C_6H_{12}O_6 \cdot H_2O$).
Lactic acid, USP, is chemically designated $CH_3CH(OH)COOH$.
Dibasic sodium phosphate, USP, is chemically designated as disodium hydrogen phosphate, dihydrate ($Na_2HPO_4 \cdot 2H_2O$)

TABLE 2 – Compartment Composition (Before Mixing)

	Compartment A (g/L)				Compartment B (g/L)			
	Calcium Chloride • $2H_2O$	Magnesium Chloride • $6H_2O$	Dextrose anhydrous (as monohydrate)	Lactic Acid	Sodium Chloride	Sodium bicarbonate	Potassium Chloride	Sodium Phosphate • $2H_2O$
PRISMASOL SOLUTIONS								
BGK 0/2.5	3.68	3.05	20 (22)	5.40	6.46	3.09	0	0
BGK 4/2.5	3.68	3.05	20 (22)	5.40	6.46	3.09	0.314	0
BGK 4/3.5	5.15	2.03	20 (22)	5.40	6.46	3.09	0.314	0
BGK 2/3.5	5.15	2.03	20 (22)	5.40	6.46	3.09	0.157	0
BGK 2/0	0	2.03	20 (22)	5.40	6.46	3.09	0.157	0
B22GK 4/0	0	3.05	20 (22)	5.40	7.07	2.21	0.314	0
BK 0/0/1.2	0	2.44	0 (0)	5.40	6.46	3.09	0	0
BGK 4/0/1.2	0	2.44	20 (22)	5.40	6.46	3.09	0.314	0
PHOXILLUM SOLUTIONS								
BK 4/2.5	3.68	3.05	0 (0)	0	6.34	3.09	0.314	0.187
B22K 4/0	0	3.05	0 (0)	0	6.95	2.21	0.314	0.187

The pH of the final solution is in the range of 7.0 to 8.5.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

PRISMASOL and PHOXILLUM solutions are pharmacologically inactive. The electrolyte concentrations in the solutions are chosen to restore plasma levels to clinically desired concentrations or maintain plasma levels at the desired concentrations.

PRISMASOL and PHOXILLUM solutions are used as replacement solution to replace water and electrolytes removed during hemofiltration and hemodiafiltration. Bicarbonate (or precursor lactate) in the solution is used as an alkalinizing buffer to restore acid-base balance to a clinically desirable level.

12.3Pharmacokinetics

The distribution of electrolytes, bicarbonate, and dextrose is determined by the patient's clinical condition, metabolic status, and residual renal function.

The elimination and replacement of water, electrolytes and buffer depend on the patient's electrolyte and acid-base balance, metabolic status, residual renal function and ongoing physiologic losses through intestinal, respiratory and cutaneous routes.

16 HOW SUPPLIED/STORAGE AND HANDLING

PHOXILLUM solutions are supplied in a two-compartment bag made of polyvinyl chloride (PVC). PRISMASOL solutions are supplied in a two-compartment bag made of either polyvinyl chloride (PVC) or polyolefin. The 5000 mL bag is composed of a small compartment (250 mL) and a large compartment (4750 mL). The two compartments are separated by a red frangible pin in the PVC bag and by a peel seal in the polyolefin bag.

The bag is overwrapped with a transparent overwrap. See Table 2 for the concentrations of the active ingredients in each compartment for each product *[see Description (11)]*.

Container	Fill Volume	NDC	Bag Type

PRISMASOL Solutions			
PRISMASOL BGK0/2.5	5000 mL	24571-108-05	PVC
PRISMASOL BGK4/2.5	5000 mL	24571-105-05	
PRISMASOL BGK4/3.5	5000 mL	24571-104-05	
PRISMASOL BGK2/3.5	5000 mL	24571-103-05	
PRISMASOL BGK2/0	5000 mL	24571-102-05	
PRISMASOL B22GK4/0	5000 mL	24571-111-05	
PRISMASOL BK0/0/1.2	5000 mL	24571-113-05	
PRISMASOL BGK4/0/1.2	5000 mL	24571-114-05	
PRISMASOL BGK0/2.5	5000 mL	24571-108-06	Polyolefin
PRISMASOL BGK4/2.5	5000 mL	24571-105-06	
PRISMASOL BGK2/3.5	5000 mL	24571-103-06	
PRISMASOL BGK2/0	5000 mL	24571-102-06	
PRISMASOL B22GK4/0	5000 mL	24571-111-06	
PRISMASOL BK0/0/1.2	5000 mL	24571-113-06	
PRISMASOL BGK4/0/1.2	5000 mL	24571-114-06	
PHOXILLUM Solutions			
PHOXILLUM BK4/2.5	5000 mL	24571-116-05	PVC
PHOXILLUM B22K4/0	5000 mL	24571-117-05	

Not all formulations may be marketed.

Storage conditions

Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15ºC to 30ºC (59ºF to 86ºF). [See USP Controlled Room Temperature]

Do not freeze or expose to excessive heat. Do not use if precipitate has formed or if container seals have been damaged.

Manufactured for:
Baxter Healthcare Corporation
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Deerfield, Illinois 60015