Package leaflet: Information for the user

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PHOXILIUM 1.2 mmol/l phosphate

Solution for haemodialysis and haemofiltration

Calcium chloride dihydrate, magnesium chloride hexahydrate, sodium chloride, sodium hydrogen carbonate, potassium chloride, disodium phosphate dihydrate

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist or nurse.
- If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

WHAT IS IN THIS LEAFLET:

1. WHAT PHOXILIUM IS AND WHAT IT IS USED FOR

Phoxilium, belonging to the group of hemofiltrates solution, contains calcium chloride dihydrate, magnesium chloride hexahydrate, sodium chloride, sodium hydrogen carbonate, potassium chloride, disodium phosphate dihydrate.

Phoxilium is used in hospitals in intensive care treatments to correct chemical imbalances in the blood which are caused by kidney injury.

The treatments, using continuous renal replacement therapy, are designed to remove accumulated waste products from the blood when the kidneys are not functioning.

The Phoxilium solution is particularly used to treat critically ill patients with acute kidney injury having:

- a normal concentration of potassium in the blood (normal kalaemia) or
- a normal or low concentration of phosphate in the blood (normal or hypophosphataemia). This medicine may also be used in case of drug poisoning or intoxications with dialysable or filterable substances.

2. WHAT YOU NEED TO KNOW BEFORE YOU USE PHOXILIUM

DO NOT USE PHOXILIUM IN THE FOLLOWING THREE CASES:

- a high concentration of potassium in the blood (hyperkalaemia)
- a high concentration of bicarbonate in the blood (metabolic alkalosis)
- a high concentration of phosphate in the blood (hyperphosphataemia)

Do not use haemodialysis or haemofiltration in any of the following three cases:

- when haemofiltration cannot correct the symptoms caused by a high blood concentration of urea (uraemic symptoms) which are the result of renal injury with pronounced hypercatabolism (an abnormally increased process of breaking down substances),
- insufficient arterial pressure in the access to the blood vessel,
- reduced clotting of the blood (systemic anticoagulation), if there is a high risk of bleeding.

WARNINGS AND PRECAUTIONS

Talk to your doctor or pharmacist or nurse before you are using Phoxilium.

Before and during treatment, your blood condition will be checked, e.g. your acid-base balance and concentrations of salts in the blood (electrolytes) will be monitored, including all fluid inputs (intravenous infusion) and outputs (urine output), even those not directly related to the therapy.

OTHER MEDICINES AND PHOXILIUM

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. This is because the concentration of other medicines may influence the treatment with Phoxilium. Your doctor will decide if any changes in the dosage of your medicines should be made.

In particular, tell your doctor if you are using either of the following:

- Additional sources of phosphate (e.g. nutritional fluids); as this may increase the risk of a high concentration of phosphate in the blood (hyperphosphataemia).
- Vitamin D and medicinal products containing calcium chloride or calcium gluconate; as they can increase the risk of a high concentration of calcium in the blood (hypercalcaemia).
- Sodium bicarbonate; as this may increase the risk of excess of bicarbonate in your blood (metabolic alkalosis).
- When citrate is used as an anticoagulant, as it can reduce plasma calcium levels.

PREGNANCY, BREAST-FEEDING AND FERTILITY

Pregnancy and breast-feeding:

There is no documented clinical data on the use of this medicine during pregnancy and lactation. This medicine should only be administered to pregnant and lactating women if clearly needed.

Fertility:

No effects on fertility are anticipated, since calcium, sodium, potassium, magnesium, chloride, hydrogen phosphate and hydrogen carbonate are normal constituents of the body.

DRIVING AND USING MACHINES

Phoxilium will not have any effect on the ability to drive or use machines.

3. HOW TO USE PHOXILIUM

Phoxilium is a product to be used in hospitals and administered by medical professionals only. The volume of Phoxilium, and therefore the dose, used will depend on your condition. The dose volume will be determined by the physician responsible for your treatment.

Phoxilium can be administered directly into the bloodstream (intravenously) through a CRRT machine or via haemodialysis, where the solution flows on one side of a dialysis membrane while the blood flows on the other side.

Always use this medicine exactly as your doctor, pharmacist or nurse has told you. Check with your doctor, pharmacist or nurse if you are not sure.

For instructions for use, please see section “The following information is intended for healthcare professionals only”.

If you use more Phoxilium than you should

Phoxilium is a product to be used in hospitals and administered by medical professionals only and your fluid balance and blood chemistry will be carefully monitored.

Therefore it is unlikely that you will use more Phoxilium than you should

In the unlikely event that an overdose occurs, your doctor will take the necessary corrective measures and adjust your dose.

Overdose may result in fluid overload, reduction of the plasma bicarbonate concentration (metabolic acidosis) and/or high phosphate concentration (hyperphosphataemia) if you are suffering from renal injury.

It could lead to severe consequences, such as congestive heart failure or disturbances in your blood chemistry.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.

THE FOLLOWING THREE SIDE EFFECTS RELATED TO THE USE OF PHOXILIUM ARE POSSIBLE:

- abnormally high or low volume of water in the body (hyper or hypovolaemia),
- changes in levels of salt in the blood (electrolyte imbalance such as hyperphosphataemia)
- Elevation of the plasma bicarbonate concentration (metabolic alkalosis) or reduction of the plasma bicarbonate concentration (metabolic acidosis).

There are also some side effects which can be caused by dialysis treatments, such as:

- nausea, vomiting, muscle cramps and low blood pressure (hypotension).

REPORTING OF SIDE EFFECTS

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via:

Malta:

ADR Reporting Website:
www.medicinesauthority.gov.mt/adrportal

Republic of Ireland:

HPRA Pharmacovigilance

Website: www.hpra.ie

United Kingdom (Northern Ireland)

The Yellow Card Scheme

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE PHOXILIUM

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and the packaging. The expiry date refers to the last day of that month.

Store between +4° - +30°C. Do not refrigerate or freeze.

Chemical and physical in-use stability of the reconstituted solution 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 be longer than 24 hours including the duration of the treatment.

Do not use this medicine if the solution is cloudy or the overwrap is damaged. All seals must be intact.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

WHAT PHOXILIUM CONTAINS.

The active substances before and after mixing (reconstitution) are shown below.

Active substances before mixing:

1000 ml of solution from the small compartment (A) contains:

Calcium chloride, 2 H_2O	3.68 g
Magnesium chloride, 6 H_2O	2.44 g

1000 ml of solution from the large compartment (B) contains:

Sodium chloride	6.44 g
Sodium hydrogen carbonate	2.92 g
Potassium chloride	0.314 g
Disodium phosphate, 2 H_2O	0.225 g

Active substances after mixing:

The solutions in the compartments A (250 ml) and B (4750 ml) are mixed to give one reconstituted solution (5000 ml) of which the composition is:

	mmol/l
Calcium, Ca^{2+}	1.25
Magnesium, Mg^{2+}	0.6
Sodium, Na^{+}	140
Chloride, Cl^{-}	115.9
Hydrogen phosphate, HPO_4^{2-}	1.2
Hydrogen carbonate, HCO_3^{-}	30
Potassium, K^{+}	4

Theoretical Osmolarity:
293 mOsm/l

The other ingredients are:

- carbon dioxide (for pH adjustment) E290,
- hydrochloric acid (for pH adjustment) E507 and
- water for injections.

WHAT PHOXILIUM LOOKS LIKE AND CONTENTS OF THE PACK

Phoxilium is a solution for haemodialysis and haemofiltration presented in a two compartment bag. The final reconstituted solution is obtained after breaking the peel seal and mixing both solutions. The reconstituted solution is clear and colourless. Each bag (A+B) contains 5000 ml solution for haemodialysis and haemofiltration. The bag is overwrapped with a transparent film.

Each box contains two bags and one package leaflet.

MARKETING AUTHORISATION HOLDER:

Republic of Ireland and Malta:
Baxter Holding B.V.
Kobaltweg 49
3542 CE Utrecht
Netherlands

United Kingdom (Northern Ireland):
Baxter Healthcare Ltd,
Caxton Way, Thetford,
Norfolk, IP24 3SE,
United Kingdom

MANUFACTURER:

Baxter Healthcare S.A.
Moneen Road,
Castlebar, Co.Mayo F23 XR63
Ireland

This medicine is authorised in the Member States of the European Economic Area and in the United Kingdom (Northern Ireland) under the following names:

Austria, Belgium, Bulgaria, Cyprus, Denmark, Estonia, Finland, France, Germany, Greece, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom (Northern Ireland): Phoxilium

Hungary: Phoxil

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03/2023

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PRECAUTIONS

The instructions for use / Handling for Phoxilium must be strictly followed.

The solutions in the two compartments must be mixed before use.

Use of a contaminated solution may cause sepsis and shock.

Phoxilium 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. Phoxilium should be inspected visually for particulate matter and discoloration prior to administration. Do not administer unless the solution is clear and the seal is intact.

The inorganic phosphate concentration should be measured regularly. Inorganic phosphate must be substituted in cases of low level of phosphate in the blood.

Additional sodium bicarbonate substitution may increase the risk of metabolic alkalosis.

In case of fluid imbalance, the clinical situation must be carefully monitored and fluid balance must be restored:

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

WARNINGS:

Phoxilium should not be used in patients with hyperkalaemia. The serum potassium concentration must be monitored before and during haemofiltration and/or haemodialysis.

Because Phoxilium is a potassium-containing solution, hyperkalemia may occur transiently after treatment is initiated. Decrease the infusion rate and confirm that the desired potassium concentration is achieved. If hyperkalaemia does not resolve, stop administration promptly.

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

Because Phoxilium is a phosphate-containing solution, hyperphosphataemia may occur transiently after treatment is initiated. The infusion rate shall be decreased until the desired phosphate concentration is achieved. If hyperphosphataemia does not resolve, the administration shall be stopped promptly.

Electrolyte and blood acid-base parameters should be monitored regularly in patients treated with Phoxilium. Phoxilium contains hydrogen phosphate, a weak acid that can influence the patient's acid-base balance. If metabolic acidosis develops or worsens during therapy with Phoxilium, the infusion rate may need to be decreased or its administration stopped.

Because Phoxilium contains no glucose, administration may lead to hypoglycaemia. Blood glucose levels should be monitored regularly in diabetic patients (including careful consideration of patients receiving insulin or other glucose lowering medications), but also considered in non-diabetic patients, e.g. risk for silent hypoglycaemia during the procedure. If hypoglycaemia develops, use of a glucose-containing solution should be considered. Other corrective measures may be necessary to maintain desired gylcaemic control.

POSOLOGY:

The volume and rate at which Phoxilium is administered depends on the blood concentration of phosphate and other 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. Administration (dose, infusion rate and cumulative volume) of Phoxilium should only be established by a physician experienced in critical care medicine and CRRT (Continuous Renal Replacement Therapy).

The dose volume is therefore at the discretion and prescription of the responsible physician.

The range of flow rates for the replacement solution in haemofiltration and haemodiafiltration are:

Adult: 500 – 3000 ml/h

The range of flow rates for the dialysate in continuous haemodialysis and continuous haemodiafiltration are:

Adult: 500 – 2500 ml/h

Commonly used combined total flow rates for CRRT (dialysate and replacement solutions) in adults are approximately 2000 to 2500 ml/h which correspond to a daily fluid volume of approximately 48 to 60 l.

PAEDIATRIC POPULATION:

In children from neonates to adolescents to 18 years, the range of flow rates used as substitution solution in haemofiltration and haemodiafiltration and as dialysis solution (dialysate) in continuous haemodialysis and continuous haemodiafiltration are 1000 to 4000 ml/h/1.73 m^2 .

For adolescents (12-18 years), the adult dose recommendation should be used when the paediatric dose is calculated to exceed the maximum adult dose.

INSTRUCTION FOR USE / HANDLING

The solution in the small compartment A is added to the solution in the large compartment B after breaking the peel seal immediately before use. The reconstituted solution shall be clear and colourless.

Aseptic technique shall be used throughout the handling and administration to the patient.

Use only if the overwrap is undamaged, all seals are intact, 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 B is fitted with an injection port for the possible addition of other necessary drugs after reconstitution of the solution. It is the responsibility of the user to judge the compatibility of an additive medication with Phoxilium by checking for eventual colour change and/or eventual precipitation, insoluble complexes or crystals. Before adding a medication, verify if it is soluble and stable in this medicine and that the pH range of Phoxilium is appropriate (pH of reconstituted solution is 7.0–8.5). Additives may be incompatible. The Instructions for Use of the medication to be added must be consulted.

Remove any fluid from the injection port, hold the bag upside down, insert the drug through the injection port and mix thoroughly. The introduction and mixing of additives must always be performed prior to connecting the solution bag to the extracorporeal circuit. The solution must be administered immediately.

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 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 either of the two access ports.

IV.a 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. (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.

IV.b 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. (See figure IV.b below)

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 solution A to solution B.

The reconstituted solution is for single use only. Discard any unused solution immediately after use.

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