Package Leaflet: Information for the user

PHOXILIAM® 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
2. What you need to know before you are given Phoxilium
3. How to use Phoxilium
4. Possible side effects
5. How to store Phoxilium
6. Contents of the pack and other information

1. What Phoxilium is and what it is used for

Phoxilium, belonging to the group of hemofilatres 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 imbalance of the blood which is caused by kidney failure.

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 failure having:
• a normal concentration of potassium in the blood (normal kalaemia) or
• a normal or low concentration of phosphate in the blood (normal or hypophosphatemia).

2. What you need to know before you are given Phoxilium

Do not use Phoxilium on patients with any of the following three conditions:
• 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 failure 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.

**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 (*hyperphosphatemia*).
• Vitamin D and medicinal products containing calcium; 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*).

**Pregnancy, breast-feeding and fertility**
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

**Driving and using machines**
Phoxilium will not have any effect on your 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*) 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 described in this leaflet or as your doctor or pharmacist or nurse have told you. Check with your doctor or 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 if you are suffering from renal failure, and 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 disturbances), and
- elevation of the plasma bicarbonate concentration (metabolic alkalosis).

There are also some side effects which can be caused by the process of haemodialysis and haemofiltration, 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, Earlsfort Terrace, IRE – Dublin 2.
Tel: +353 1 6764971, Fax: +353 1 6762517, Website: www.hpra.ie;
E-mail: medsafety@hpra.ie

**UK**
Yellow Card Scheme
www.mhra.gov.uk/yellowcard

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.

Do not use this medicine if the solution is cloudy or the over wrap 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 H₂O: 3.68 g
- Magnesium chloride, 6 H₂O: 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 H₂O: 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:

<table>
<thead>
<tr>
<th>Substance</th>
<th>mmol/l</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium, Ca²⁺</td>
<td>1.25</td>
</tr>
<tr>
<td>Magnesium, Mg²⁺</td>
<td>0.6</td>
</tr>
<tr>
<td>Sodium, Na⁺</td>
<td>140</td>
</tr>
<tr>
<td>Chloride, Cl⁻</td>
<td>115.9</td>
</tr>
<tr>
<td>Hydrogen phosphate, HPO₄²⁻</td>
<td>1.2</td>
</tr>
<tr>
<td>Hydrogen carbonate, HCO₃⁻</td>
<td>30</td>
</tr>
<tr>
<td>Potassium, K⁺</td>
<td>4</td>
</tr>
</tbody>
</table>

Theoretical Osmolarity: 293 mOsm/l
The other ingredients are:
- carbon dioxide (for pH adjustment),
- hydrochloric acid (for pH adjustment) 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 frangible pin 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 over wrapped with a transparent film. Each box contains two bags and one package leaflet.

Marketing Authorisation Holder:
Gambro Lundia AB, Magistratsvägen 16, SE-226 43 Lund, SWEDEN

Manufacturer:
Gambro Dasco S.p.A. Sondalo Plant, Via Stelvio 94, 23035 Sondalo (SO), ITALY

This medicinal product is authorised in the Member States of the EEA 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: Phoxilium

Hungary: Phoxil

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The following information is intended for healthcare professionals only

Phoxilium 1.2 mmol/l phosphate
Solution for haemodialysis and haemofiltration

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.

Carefully follow the instructions for use/handling.

Solution A must be mixed with solution B before use to obtain the reconstituted solution suitable for haemofiltration or continuous haemodialysis.
If heating of the solution to body temperature (37°C) is necessary the procedure must be carefully controlled verifying that the solution is clear and without particles.

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.

The volume of Phoxilium used will depend on the patient’s clinical condition and the target fluid balance. Continued application of haemofiltration will remove excess fluid and electrolytes. In case of fluid imbalance, the clinical situation must be carefully monitored and fluid balance must be restored:
• In case of hypervolaemia, 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.

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

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.

The use of contaminated haemofiltration and haemodialysis solution may cause sepsis and shock.

The range of flow rates for the replacement solution in haemofiltration and haemodiafiltration are:
Adult and adolescents: 500 – 3000 ml/hour
Children: 15 – 35 ml/kg/hour

The range of 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

**Instruction for use / Handling**
The solution is packaged in a two compartment bag.
Aseptic technique should be used throughout the administration to the patient.
Use only if the solution is clear and the over wrap is undamaged. All seals must be intact. 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.
Drugs should only be added to the solution under the responsibility of a physician in the following way:
Remove any fluid from the injection port, hold the bag upside down, insert the drug through the injection port and mix thoroughly. **The solution must be administered immediately.**

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. (See figure I below)

II  Make sure all the fluid from the small compartment A is transferred into the large compartment B. (See figure II below)

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. (See figure III below)

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. (See figure IV below)

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

V.a  If the luer access is used, using aseptic technique, remove the cap and connect the male luer lock on the dialysis or replacement line to the female luer receptor on the bag; tighten. Using both hands, break the blue 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. (See figure V.a below)

V.b  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 V.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.