Biphozyl

DXXXXXXXX Rev. 2014-10/1 REG **XXXX**

GAMBRO®

Biphozyl
Solution for haemodialysis / haemofiltration
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, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

WHAT IS IN THIS LEAFLET

1. WHAT BIPHOZYL IS AND WHAT IT IS USED FOR

This medicine is a solution for dialysis treatment (haemofiltration, haemodialysis and haemodiafiltration) which is used to remove waste products from the blood when the kidneys are not functioning. This medicine is used in hospitals during intensive care treatment using Continuous Renal Replacement Therapy (CRRT). This medicine is particularly used to treat critically ill patients with acute kidney injury having:
- a normal concentration of potassium (normal kalaemia) in the blood
- a normal pH in the blood
- a normal or low concentration of phosphate (normal or hypophosphataemia) in the blood
- a high concentration of calcium (hypercalcaemia) in the blood

2. WHAT YOU NEED TO KNOW BEFORE YOU USE BIPHOZYL

DO NOT USE BIPHOZYL IN CASE OF:
- allergy to one of the active substances or any of the other ingredients (listed in section 6)
- a low concentration of calcium (hypocalcaemia) in the blood
- a high concentration of potassium (hyperkalaemia) in the blood
- a high concentration of phosphate (hyperphosphataemia) in the blood

WARNINGS AND PRECAUTIONS

Warnings
Talk to your doctor, pharmacist or nurse before using Biphozyl.

Use only if the solution is clear and free from visible particles.

The instructions for use must be strictly followed.

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

Use only with a dialysis machine for CRRT.

Use only if the overwrap and solution bag are undamaged. All seals must be intact. Use of a contaminated solution may cause sepsis and shock.

Incorrect use of the access ports or other restrictions to fluid flow might lead to incorrect patient weight loss and may result in machine alarms. Continuing treatment without resolving the originating cause may result in patient injury or death.

Precautions
This medicine is calcium free and could cause hypocalcaemia. Infusion of calcium might be necessary.

If heating of the solution to body temperature (+37°C) is necessary the procedure must be carefully controlled. It should be verified that the solution is clear and without particles prior to administration. If not, discard the solution.

Your doctor will closely monitor your haemodynamic status, fluid balance, electrolyte and acid-base balance throughout the procedure.

This medicine has a hydrogen carbonate content at the lower end of the normal concentration range in the blood. This is appropriate when using citrate anticoagulation, as citrate is metabolized to hydrogen carbonate, or when normal pH values have been restored. Assessment of buffer needs, through repeated blood pH measurement and review of the overall therapy, is mandatory. A solution with higher hydrogen carbonate content may be required.

In case of abnormally high volume of fluid in the body (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 abnormally low volume of fluid in the body (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 and/or dialysate can be increased.

Children
No specific adverse effect on children is expected when using this medicine.

Older people
No specific adverse effect on older people is expected when using this medicine.

Other medicines and Biphozyl
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines including medicines obtained without a prescription. This is because the concentration of other medicines may be reduced during dialysis treatment. Your doctor will decide if any changes in the dosage of your medicines should be made.

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 sodium, potassium, magnesium, chloride, hydrogen phosphate and hydrogen carbonate are normal constituents of the body.

Driving and using machines
This medicine is not known to affect your ability to drive or use machines.

3. HOW TO USE BIPHOZYL

For intravenous use and use in haemodialysis. This medicine is to be used in hospitals and administered by medical professionals only. The volume used, and therefore the dose of this medicine, will depend on your condition. The dose volume will be determined by your doctor.

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.

It is the responsibility of the physician to determine the compatibility of an additive medication with this medicine by checking for possible colour change and/or possible precipitation. Before adding a medication, verify if it is soluble and stable in this medicine.

POSOLOGY
The range of flow rates when used as replacement solution in haemofiltration and haemodiafiltration are:

Adult and adolescents:	500 – 3000 ml/h
Children:	15 – 35 ml/kg/h

The range of flow rates when used as dialysis fluid (dialysate) in continuous haemodialysis and continuous haemodiafiltration are:

Adult and adolescents:	500 – 2500 ml/h
Children:	15 – 30 ml/kg/h

INSTRUCTIONS FOR USE
This medicine will be given to you in a hospital. Your doctor will know how to use it.

For instructions for use see the end of this leaflet.

IF YOU USE MORE OF BIPHOZYL THAN YOU SHOULD
Contact your doctor or nurse immediately if you have taken more of this medicine than recommended in this package leaflet or than prescribed by your doctor and you feel uncomfortable.

The symptoms of overdose are tiredness, oedema or shortness of breath.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them. Your blood tests and clinical condition will be regularly monitored by a doctor or nurse in order to find possible side effects. Use of this solution could cause:

- Changes of levels of salts in the blood (electrolyte imbalances) such as: low calcium level (hypocalcaemia), high potassium level (hyperkalaemia) and high phosphate level (hyperphosphataemia)

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

- Abnormally high (hypervolaemia) or low volume (hypovolaemia) of fluid in the body
- Decreased blood pressure
- Nausea, vomiting
- Cramps

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

You can also report side effects directly:

United Kingdom:
Via the Yellow Card Scheme at:
www.mhra.gov.uk/yellowcard

Republic of Ireland:
Via HPRA Pharmacovigilance,
Earlsfort Terrace, IRL - Dublin 2;
Tel: +353 1 6764971;
Fax: +353 1 6762517;
Website: www.hpra.ie;
E-mail: medsafety@hpra.ie

Malta:
Via The Medicines Authority, Post-Licensing Directorate, 203, Level 3, Rue D'Argens, GZR 1368 Gzira
Website:
www.medicinesauthority.gov.mt
Email:
postlicensing.medicinesauthority@gov.mt

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

5. HOW TO STORE BIPHOZYL

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.

This medicinal product does not require any special storage conditions.

Do not 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.

This medicine is for single use only. Any unused solution must be discarded.

The solution can be disposed of via wastewater without harming the environment.

Do not use this medicine if you notice damage to the product or visible particles in the solution. All seals must be intact.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

WHAT BIPHOZYL CONTAINS

Before reconstitution
In the small compartment A (250 ml):

Magnesium chloride hexahydrate	3.05 g/l

In the large compartment B (4750 ml):

Sodium chloride	7.01 g/l
Sodium hydrogen carbonate	2.12 g/l
Potassium chloride	0.314 g/l
Disodium phosphate dihydrate	0.187 g/l

After reconstitution
The reconstituted solution, A+B:
Active substances

	mmol/l	mEq/l
Sodium, Na^+	140	140
Potassium, K^+	4	4
Magnesium, Mg^{2+}	0.75	1.5
Chloride, Cl^-	122	122
Hydrogen phosphate, HPO_4^{2-}	1	2
Hydrogen carbonate, HCO_3^-	22	22

Theoretical osmolarity: 290 mOsm/l
pH: 7.0 – 8.0

The other ingredients are:

- Dilute hydrochloric acid (for pH adjustment) E 507
- Water for injections
- Carbon dioxide (for pH adjustment) E 290

WHAT BIPHOZYL LOOKS LIKE AND CONTENTS OF THE PACK

This medicine is a solution for haemodialysis / haemofiltration and is packed in a two-compartment bag of a multilayer film containing polyolefins and elastomers. The final solution is obtained after opening the peel seal and mixing the solutions in the small and large compartments. The solution is clear and colourless. Each bag contains 5000 ml solution and the bag is overwrapped with a transparent film. Each box contains two bags and one package leaflet.

MARKETING AUTHORISATION HOLDER

Gambro Lundia AB
Magistratsvägen 16
226 43 Lund
Sweden

MANUFACTURER

Gambro Dasco S.p.A.
Via Stelvio, 94
23035 Sondalo (SO)
Italy

For further information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

LOCAL REPRESENTATIVE

Malta:
Associated Equipment Ltd
Lourdes Square
Rihan Avenue
San Gwann SGN2100
Malta

UK & Ireland:
Gambro Lundia AB
Lundia House
3 The Forum
Minerva Business Park
Peterborough, PE2 6FT
United Kingdom

This medicinal product is authorised in the Member States of the EEA under the following names:
Biphozyl.

This leaflet was last revised in <{10/2014}>

POSOLOGY

The volume of Biphozyl to be used will depend on the clinical condition of the patient, target electrolyte and fluid balance, buffer need and other solutions that may be needed concomitantly.

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

The range of flow rates when used as replacement solution in haemofiltration and haemodiafiltration are:

Adult and adolescents:	500 – 3000 ml/h
Children:	15 – 35 ml/kg/h

The range of flow rates when used as dialysis fluid (dialysate) in continuous haemodialysis and continuous haemodiafiltration are:

Adult and adolescents:	500 – 2500 ml/h
Children:	15 – 30 ml/kg/h

Commonly used flow rates in adults are approximately 2000 ml/h which correspond to a daily replacement fluid volume of approximately 20-25 ml/kg/h.

Paediatric population
Children < 16 years of age:
Evidence from clinical studies and experience suggests that use in the paediatric population is not associated with differences in safety or effectiveness.

Older people
Adults > 65 years of age:
Evidence from clinical studies and experience suggests that use in the elderly population is not associated with differences in safety or effectiveness.

OVERDOSE

SYMPTOMS OF OVERDOSE

Overdose of Biphozyl can lead to severe clinical condition, such as congestive heart failure, electrolyte or acid-base disturbances.

TREATMENT OF OVERDOSE

Hypervolaemia
Overdose resulting in fluid overload with pulmonary oedema and other signs of congestive heart failure can occur in patients with acute or chronic renal failure. Continuation of treatment with haemodialysis, haemofiltration or haemodiafiltration can be used to increase the volume of fluid removal by means of ultrafiltration, to restore normal fluid balance and thus correct the overdose. Thus in cases 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.

Hypovolaemia
In cases of severe hypovolaemia during haemofiltration or haemodiafiltration, 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.

PREPARATION AND/OR HANDLING

Remove the overwrap from the bag immediately before use.
Aseptic technique should be used throughout administration to the patient. The solution should be used immediately after opening to avoid microbiological contamination.

I Open the seal by holding the small compartment with both hands and squeezing it until an opening is created in the peel seal between the two compartments. (See figure I below.)

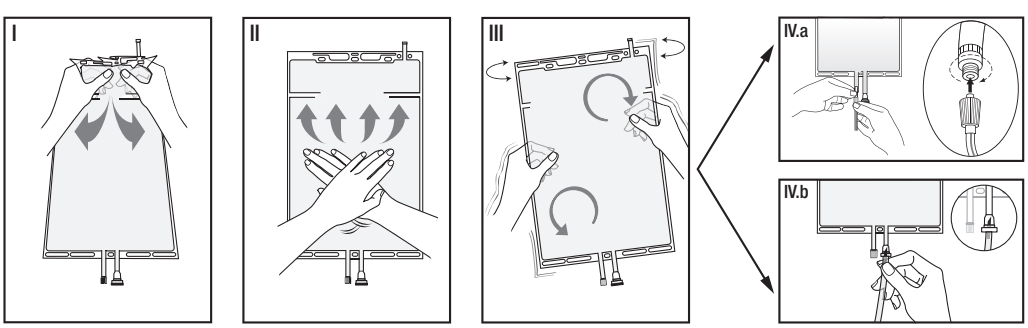
II Push with both hands on the large compartment until the peel seal between the two compartments is entirely open. (See figure II below.)

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 connector 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 connector 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 connector (or spike connector) is used, first remove the snap-off cap. Introduce the spike through the rubber septum. Verify that the fluid is flowing freely. (See figure IV.b below.)



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