IRISH MEDICINES BOARD ACTS 1995 AND 2006

MEDICINAL PRODUCTS(CONTROL OF PLACING ON THE MARKET)REGULATIONS,2007

(S.I. No.540 of 2007)

PA0167/104/002
Case No: 2044285

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Baxter Healthcare Limited

Caxton Way, **Thetford**, **Norfolk IP24 3SE**, **United Kingdom**

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Monosol-K with 4 mEq Potassium/l. Solution for haemodialysis, haemodiafiltration and haemofiltration

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **08/06/2008**.

Signed on behalf of the Irish Medicines Board this

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A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Monosol-K with 4 mEq Potassium/l
Solution for haemodialysis, haemodiafiltration and haemofiltration

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition in g/l

Glucose monohydrate	1.1	g/l
Sodium chloride	6.43	g/l
Potassium chloride	0.298	g/l
Calcium chloride ($2H_2O$)	0.257	g/l
Magnesium chloride ($6H_2O$)	0.152	g/l
Sodium lactate	3.36	g/l

Composition in mmol/l

Sodium	140	mmol/l
Potassium	4	mmol/l
Magnesium	0.75	mmol/l
Calcium	1.75	mmol/l
Chloride	119	mmol/l
Lactate	30	mmo/l
Glucose	5.55	mmol/l
Osmolarity	301	mOsm/l

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for haemodialysis, haemodiafiltration and haemofiltration
Monosol-K with 4 mEq Potassium/l is a sterile, non-pyrogenic, clear solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As substitution solution in continuous haemofiltration and haemodiafiltration and as dialysis solution in continuous haemodialysis and haemodiafiltration for acute renal failure.

4.2 Posology and method of administration

Substitution fluid may be infused either in pre or post-dilutional mode, according to the physician’s prescription. The amount of substitution fluid is determined so as to ensure a proper negative balance, according to each individual case, between the fluids infused and the fluids lost by ultrafiltration.

The solution can be used as a dialysate fluid with any type of dialysis membrane or fluid with any type of dialysis membrane or hemofilter.

Dialysate fluid must be properly circulated from dialysate inlet to dialysate outlet, as in conventional haemodialysis. The usual dialysate flow rate in CAVHD or CVVHD is much lower than in conventional dialysis, ranging from 15 ml/min to 30 ml/min.

Administration
- Haemodialysis: via the dialysis compartment of the dialyser.
- Haemofiltration: via the arterial or venous blood line.

4.3 Contraindications

Solution dependent contra-indications:
- Hyperkalaemia,
- Severe metabolic acidosis,
- Impaired metabolism of lactate.

Haemofiltration / haemodialysis dependent contra-indications:
- Inadequate blood flow from vascular access,
- All states with elevated risk of haemorrhage on account of systemic anticoagulation.

4.4 Special warnings and precautions for use

- These solutions are to be used only by or under the direction of a physician who should have a sound experience of intensive care nursing and/or haemofiltration and haemodiafiltration techniques.

- When using, high volumes of fluid, either as a replacement fluid or dialysate, consideration should be given to the fact that the lactate uptake to blood may exceed the metabolic capabilities to convert it into bicarbonate.

- Very special care must be devoted to ensuring proper fluid balance. An accurate fluid balance record must be kept and the weight of the patient must be closely monitored to avoid fluid balance problems which may lead to life-threatening complications such as congestive heart failure or hypovolaemic shock due to excessive volume depletion.

- Close monitoring of kalaemia must be performed to enable selection of the appropriate potassium concentration and thus avoid hyperkalaemia or hypokalaemia.

- Special attention must be paid to acid-base equilibium, especially in those patients with liver impairment and cardiogenic shock. Serum lactate and pH must be closely monitored.

- Glycaemia, phosphataemia, calcaemia and magnesaemia should also be frequently monitored, together with the levels of urea and other waste products.

- Care should be taken when the solution is used in patients with hypercatabolism associated with acute renal failure, hepatic insufficiency with lactate acidosis and serious cardiac insufficiency.

- Due to the fact that the solution may be infused into the blood path of the extracorporeal circuit, special care must be devoted to keeping the infusion path sterile. The dialysate circuit must also be kept sterile, since backfiltration may easily occur in CAVHD, CVVHD, CAVHDF and CVVHDF.

4.5 Interaction with other medicinal products and other forms of interaction

When prescribing the solution to be used for an individual patient, consideration should be given to the potential interaction between treatment with Monosol and therapy directed at other existing illnesses. For example: rapid potassium removal may create arrhythmias in cardiac patients using digitalis or similar drugs; digitalis toxicity may be asked by elevated potassium or magnesium, and by hypocalcaemia. Correction of electrolytes may precipitate signs and symptoms of digitalis excess.

Conversely, toxicity may occur at suboptimal doses of digitalis if potassium is low or calcium is high.
Chloride plasma levels should be monitored as the chloride concentration in the solution is higher than in normal plasma.
Diabetics require careful monitoring of insulin requirements during and following treatment with glucose containing solutions.

4.6 Pregnancy and lactation

The safety of these solutions for use in human pregnancy has not been established. These solutions should only be administered to pregnant women if clearly needed.

4.7 Effects on ability to drive and use machines

Not applicable.

4.8 Undesirable effects

The undesirable effects below listed reflect the type of undesirable effects that may be reported with haemofiltration or haemodialysis solutions.

System Organ Class	Preferred Term
Metabolism and nutrition disorders	Electrolyte imbalance
	Fluid imbalance
	Hypervolaemia
	Hypovolaemia
Vascular disorders	Hypertension
	Hypotension
Musculoskeletal, connective tissue and bone disorders	Muscle cramping

4.9 Overdose

The infusion rate of the substitution fluid should be properly prescribed in order to obtain an appropriate fluid, electrolyte and acid/ base balance and to avoid fluid overload.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Haemodialytics and Haemofiltrates (B05Z)
As dialysates, the solutions remove metabolic waste products and help to manage serum electrolyte and / or fluid imbalances during continuous renal replacement therapies in the treatment of acute renal failure. As a replacement fluid the solution serves as an alkalinising agent and provides a continuous source of water for hydration, electrolytes and calories.

5.2 Pharmacokinetic properties

Insignificant amounts of the solutions are absorbed by patients utilising them as dialysates. There is only an exchange between the dialysate and the patient's serum resulting in the removal of excess body fluid, electrolytes and metabolic waste products.
Solution used to adjust blood volume is absorbed directly into the blood stream where each component of the solution is essential in the maintenance of homeostasis.
Most of the components of the solution are excreted predominantly in the urine; consequently, during acute renal failure, normal extracellular fluid levels of each product component must be maintained trough the use of continuous renal replacement therapies. Lactate is a biological precursor of bicarbonate.

5.3 Preclinical safety data

All ingredients are physiological components in animal and human plasma. Within the therapeutic dosage range toxic effects are not to be expected under the condition of clinical application.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections

6.2 Incompatibilities

- Additives should not be added to the solution when acting as a dialysate fluid.
- Additives may be added to the solution when acting as a substitution fluid, but only those additives for which compatibility has been documented should be used.
- Never add bicarbonate to the solution as precipitation of calcium and magnesium carbonate will occur.
- Bicarbonate solutions, if required, must be infused separately.

6.3 Shelf Life

The shelf life is 2 years in the overpouch.
The product, once removed from its individual overpouch, should be used immediately.

6.4 Special precautions for storage

Do not store above 25°C. Do not refrigerate or freeze.

6.5 Nature and contents of container

The solution is packaged in flexible plasticised (poly vinyl chloride) bags of 5000 ml size, containing 5000 ml of solution. Each unit is sealed inside a high density polyethylene overpouch.

Pack size:
Each box contains two single 5 L bags.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

- Follow directions of attending physician and package leaflet accompanying the product.

- Remove the container from the overwrap.

- Check for minute leaks by squeezing the bag firmly. If leaks are found discard the solution as sterility may be impaired. Occasionally condensation does occur between the overpouch and the bag due to the manufacturing process and is not necessarily indicative of a leak. In addition, do not use the solution if the fluid is cloudy or the blue tip protector is missing.

- If the resealable rubber plug on the medication port is missing or partially removed, do not use product if medication is to be added.

- Once the bag has been removed from the overpouch, it should be used immediately.

- Remove the blue tip protector from the port, hang the bag onto either a drip stand or weighing scales (if using an automated machine) and insert the giving set into the bag.

- The product is for single use only.

- Discard any damaged or partially used container.

7 MARKETING AUTHORISATION HOLDER

Baxter Healthcare Ltd.
Caxton Way
Thetford
Norfolk IP24 3SE
United Kingdom

8 MARKETING AUTHORISATION NUMBER

PA 167/104/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 26 November 1999

Date of last renewal: 08 June 2008

10 DATE OF REVISION OF THE TEXT

March 2010