Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Accusol 35 Potassium 4 mmol/lSolution for haemofiltration, haemodialysis and haemodiafiltration

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Composition	**Per 1000 ml Accusol 35**
Large chamber 'A'	
Calcium chloride dihydrate	0.343 g
Magnesium chloride hexahydrate	0.136 g
Sodium chloride Potassium chloride Glucose monohydrate	7.52 g 0.398g 1.47g
Small chamber 'B'	
Sodium bicarbonate	13.4 g

Final solution after mixing	**Per 1000 ml Accusol 35**
Calcium chloride dihydrate	0.257 g
Magnesium chloride hexahydrate	0.102 g
Sodium chloride	6.12 g
Sodium bicarbonate Potassium chloride Glucose anhydrous	2.94 g 0.298g 1.0g

Equivalent to the following ionic composition:

Ionic Composition of Final Solution	**Per 1000 ml Accusol 35**
Calcium (Ca^{++})	1.75 mmol
Magnesium (Mg^{++})	0.5 mmol
Sodium (Na^{+})	140 mmol
Potassium ($K^{+)}$ Chloride (Cl^{-}) Glucose anhydrous	4mmol 113.3 mmol 5.55mmol
Bicarbonate (HCO_3^{-})	35 mmol
Theoretical osmolarity	**300 mOsm/l**

The 5000 ml of final solution results from the mixing of 3750 ml of solution 'A' with 1250 ml of solution 'B'.

The pH of the final solution is between 7.0 -7.5.

For the full list of excipients, see section 6.1.

The number "35" in the name specifies the buffer concentration of the solution (bicarbonate = 35 mmol/l).

3 PHARMACEUTICAL FORM

Solution for haemofiltration, haemodialysis and haemodiafiltration.
Accusol 35 is a sterile, non pyrogenic, clear and colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Accusol 35 is indicated for the treatment of acute and chronic renal failure, as substitution solution in haemofiltration and haemodiafiltration, and as dialysis solution in haemodialysis and haemodiafiltration.

Accusol 35, Potassium4 mmol/l is primarily intended for usein patients with hypokalaemia.

4.2 Posology and method of administration

For haemofiltration, haemodialysis and haemodiafiltration.

Accusol 35 as substitution solution
The amount of substitution solution to be administered in adults is determined by the ultrafiltration rate and is set for each individual case to ensure an adequate electrolyte fluid balance.

Adults:

- Chronic renal failure: 7 to 35 ml/kg/hr,
- Acute renal failure: 20 to 35 ml/kg/hr,

Elderly: as for adults

These fluid volume recommendations may be adjusted by the prescribing physician according to the patient's clinical status.

Accusol 35 can be administered into the extracorporeal blood circuit either in pre- and/or post- dilution mode according to the physician's prescription.

Accusol 35 as dialysis solution
The prescription and amount of dialysis solution depend upon the mode of therapy, frequency and duration of treatment and will be selected by the prescribing physician according to the patient's clinical status.

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

After removal of the overpouch, immediately open the long-seal (interchamber seal) to mix the two solutions and then open the short SafetyMoon seal (seal near access port) to allow administration of the mixed solution. For instructions for use and handling, please refer to section 6.6.

4.3 Contraindications

Solution dependent contraindications

- Hyperkalaemia.
- Metabolic alkalosis.

Haemofiltration / haemodialysis/ haemodiafiltration dependent contraindication due to the technical procedure itself:

- Renal failure with increased hypercatabolism in cases where uraemic symptoms can no longer be relieved by haemofiltration.
- Inadequate blood flow from vascular access.
- If there is a high risk of haemorrhage on account of systemic anticoagulation.

4.4 Special warnings and precautions for use

- Accusol 35 solution must only be used by or under the direction of a physician experienced in haemofiltration, haemodialysis or haemodiafiltration techniques,

- Rarely, precipitation of the solution may occur several hours after the start of therapy and if precipitate is formed, the Accusol 35 solution and CRRT tubing lines must be replaced immediately and the patient carefully monitored.
- Fluid balance must be carefully monitored,
- Acid-base balance must be carefully monitored,
- Similarly, electrolyte balance (chloraemia, phosphataemia, calcaemia, magnesaemia and natraemia) should be monitored regularly to detect any potential imbalance,
- Kalaemia must be monitored regularly before and during treatment. If hypokalaemia is present or starts to develop, supplementation of potassium may be required. If hyperkalaemia starts to develop, an increase in the filtration rate and/or changing to a substitution solution with a lower potassium concentration may be indicated as well as usual measures of intensive care medicine,
- Blood glucose levels must be monitored closely, especially in diabetic patients,
- In case the long-seal (interchamber seal) is not opened (i.e. only short SafetyMoon seal near access port opens) and the solution of the small chamber "B" is given, alkalosis may arise. Most common clinical signs / symptoms of alkalosis are nausea, lethargy, headache, arrhythmia, respiratory depression.

4.5 Interaction with other medicinal products and other forms of interactions

When prescribing Accusol 35 Potassium 4 mmol/l, consideration should be given to the potential interactions between this treatment and other concomitant therapies related to other pre-existing conditions.

- Blood concentration of other medicinal products may be altered during haemodialysis, haemofiltration and haemodiafiltration.
- Plasma levels of potassium in patients using cardiac glycosides must be carefully monitored due to an increased risk of hypokalaemia associated arrhythmias.
- Vitamin D and medicinal products containing calcium can increase the risk of hypercalcaemia (eg calcium carbonate acting as a chelator of potassium).
- The additional substitution of sodium bicarbonate can increase the risk of metabolic alkalosis.

4.6 Fertility, pregnancy and lactation

There are no preclinical or clinical data on the use of Accusol 35 during pregnancy and lactation. Accusol 35 should only be administered to pregnant and lactating women if clearly needed.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The undesirable effects reported are based on adverse event reports from clinical trials (see (1) below), which were assessed by the investigator to be related to Accusol, as well as from a literature review (see (2) below).
The frequency has been evaluated by using the following criteria: very common (> 1/10), common (> 1/100, <1/10), uncommon (> 1/1,000, <1/100), rare (> 1/10,000, < 1/1,000) and very rare (< 1/10,000).

1) Clinical Trials

System Organ Class	Adverse Drug Reaction	Frequency	Procedure related	Solution related
Metabolic and Nutritional	Hypoglycaemia NOS	Rare	Yes	Yes

2) Literature review

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

- Potential adverse reactions related to the treatment may include nausea, vomiting, muscle cramps, hypotension, bleeding, clotting, infection and air embolism.

- Potential adverse reactions related to the product may include metabolic alkalosis, electrolyte disturbances and/or fluid imbalances: hypophosphataemia, hypoglycaemia, hypo- and hypervolaemia, hypo- and hypertension.

Reporting suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: http://www.hpra.ie/; E-mail: medsafety@hpra.ie

4.9 Overdose

Overdose should not occur if the fluid and electrolyte balances are monitored regularly as recommended in section 4.4.
Overdose may lead to hypervolaemia and electrolyte disturbances. These symptoms can be corrected by adjusting the ultrafiltration rate and the volume of solution administered.
Electrolyte imbalances should be managed according to the specific electrolyte disturbance.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Haemofiltrates, ATC code: B05Z B
Accusol 35is pharmacologically inactive. The solution consists of ions that are present at concentrations similar to physiological level in plasma.
As substitution solution, Accusol 35 provides a continuous source of electrolytes and water for hydration and acts as an alkalinising agent.
As dialysis solution, Accusol 35 removes metabolic waste products from the blood and helps to manage the serum electrolytes and/or fluid imbalances.

5.2 Pharmacokinetic properties

Not relevant as the active ingredients of Accusol 35 are pharmacologically inactive and near to physiological plasma concentrations.

5.3 Preclinical safety data

There are no preclinical data considered relevant to clinical safety beyond data included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections,
Hydrochloric acid (pH adjuster),
Sodium hydroxide (pH adjuster)
Disodium phosphate dihydrate

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Shelf life
24 months when stored in the overpouch.

Shelf life after mixing
Accusol 35, once removed from the overpouch and mixed should be used within 24 hours.

6.4 Special precautions for storage

Do not refrigerate or freeze

6.5 Nature and contents of container

Accusol 35 is stored in a non PVC two-chamber bag made of a coextruded film of Polypropylene, Polyamide and a blend of Polypropylene, SEBS and Polyethylene (Clear-Flex). A long-seal (interchamber seal) separates the two chambers.
The large chamber 'A' is fitted with a medication port and the small chamber 'B' is fitted with an access port for connection to a suitable administration set. . A short SafetyMoon seal (seal near access port) needs to be opened to allow administration of the mixed solution.

The two-chamber bag is presented in a protective transparent overpouch made of copolymers.
The volume of the container after mixing is 5000 ml (3750 ml in the large chamber and 1250 ml in the small chamber).
Accusol 35 is available as 2 x 5000 ml per box.

6.6 Special precautions for disposal and other handling

- Check the integrity of the product. If one of the seals is opened prematurely, do not use the bag. In case of damage, discard the container.
- Do not administer unless the solution is clear.
- Aseptic technique should be observed throughout the whole procedure.
- Concomitant drugs may be added through the medication port in the larger chamber. Drug compatibility must be checked before admixture. Add the medication and activate the long-seal (inter-chamber seal) immediately. The product must be used immediately after any drug addition.
- After removal of the overpouch, immediately open the long-seal (interchamber seal) to mix the two solutions. Ensure the long-seal (interchamber seal) is completely activated and the two solutions are completely mixed. Then open the short Safety Moon seal (seal near access port) to allow administration of the mixed solution. Connect to the patient line and activate the access port. The solution must be used within 24 hours of mixing.
- Discard any unused remaining solution.
- For single use only.
- Use Accusol 35 only with adequate equipment able to monitor the therapy.

7 MARKETING AUTHORISATION HOLDER

Nikkiso Belgium bvba
Industriepark 6
3300 Tienen
Belgium

8 MARKETING AUTHORISATION NUMBER

PA2021/002/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28th April 2006
Date of last renewal: 28th March 2015

10 DATE OF REVISION OF THE TEXT

January 2018