Package leaflet: Information for the user

Accusol 35, Solution for haemofiltration, haemodialysis and haemodiafiltration

Read all of this leaflet carefully before you are given 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.
- If you get any side effects talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Accusol 35 is and what it is used for

Accusol 35 is a solution for haemofiltration, haemodialysis and haemodiafiltration.

Accusol 35 is prescribed to you if you have temporary or permanent kidney failure.

It purifies your blood of waste products; it corrects the acidity or alkalinity and the level of salts in your blood. As a replacement fluid in haemodiafiltration and haemofiltration, it can also be used as a source of salts and water for hydration.

Accusol 35 solutions are supplied in a non-PVC bag with two chambers. The two chambers are separated by a long- seal (interchamber seal). Prior to use, the two chambers of Accusol 35 solutions must first be mixed by activating the long-seal (interchamber seal), followed by the activation of the short SafetyMoon seal near the access port.

Accusol 35 may be given to you, especially if you have a high level of potassium.

Accusol 35 solutions must only be used by or under the direction of a doctor.

2. What you need to know before you are given Accusol 35

Before starting the therapy, your doctor will ensure that you have a good access to your vein and artery. He will also ensure that you do not present a high risk of bleeding.

Accusol 35 solutions are available in different potassium and glucose concentrations. Your blood levels of potassium and glucose will be monitored very closely to ensure that the most appropriate Accusol 35 formulation is used.

Your doctor will not give you Accusol 35:

- if you do not have a good access to the veins and/or arteries.
- if you have an excessive risk of bleeding.
- if you have a high level of bicarbonate in your blood.
- if you have a potassium blood level too low, unless you are simultaneously receiving potassium supplementation.
- if you have a clinical condition whereby the current acidity or alkalinity of your blood may worsen.
- if you have kidney failure where waste products cannot be removed from the blood stream by haemofiltration.

Warnings and precautions

Accusol 35 can only be used by or under the direction of a doctor who has experience with haemofiltration, haemodialysis or haemodiafiltration techniques.

Your doctor will

- measure the acidity, different salts and waste product levels in your blood.
- ensure that their levels are correct and closely monitored during your treatment.
- ensure that the fluid balance of your body is well maintained.
- check your blood glucose very carefully especially if you are diabetic.
- measure the potassium level in your blood regularly.
- ensure, just before use, the contents of the two chambers are mixed by activating the long-seal (interchamber seal), followed by the short SafetyMoon seal near the access port. If your doctor infuses unmixed solution, your blood bicarbonate level may increase. This may cause side effects such as nausea, drowsiness, headache, abnormal heartbeat and difficulty of breathing.

Other medicines and Accusol 35

Tell your doctor if you are taking, have recently taken or might take any other medicines.

Taking Accusol 35 may affect and interact with other medicines.

- If you take Vitamin D or medicines containing calcium, your blood calcium level may be modified.
- If you take additional sodium bicarbonate, there is an increased risk of abnormal salt and alkali levels (alkalosis) in your blood.
- If you use medicines for the heart known as cardiac glycosides you may need potassium supplements. Your doctor will monitor you closely during treatment.

Pregnancy and breast-feeding

Tell your doctor if you are pregnant or breast-feeding. He will determine the benefits versus the risks of using Accusol 35.

3. How you will be given Accusol 35

Depending on your therapy, your doctor will administer Accusol 35 by way of the tubing from the dialysis machine.

The treatment by haemofiltration, haemodialysis or haemodiafiltration that you receive will depend upon your clinical diagnosis, physical examination, laboratory results and response to treatment.

Your doctor will determine the right formulation and amount of Accusol 35 solutions for your clinical condition.

How much and how often?

Your doctor will decide and adjust the flow rate and volume of the solution to be administered.

The amount of fluid required depends upon how Accusol 35 is being used.

If you are adult or elderly and

- treated for chronic renal failure with Accusol 35 as substitution solution**,** you should receive 7 to 35 ml/kg/hr or more.
- treated for temporary kidney failure with Accusol 35 as substitution solution**,** you should receive 20 to 35 ml/kg/hr or more.
- treated for chronic or temporary kidney failure with Accusol 35 as dialysis solution, the amount of solution will be determined by frequency and duration of treatment.

4. Possible side effects

Like all medicines this medicine can cause side effects, but not everyone gets them.

Possible rare side effects *(occurring in less than 1 in 1000 patients)* of Accusol 35 may include

- Low blood glucose (hypoglycaemia).

You may experience other possible side effects. They may not all be due to the solutions or treatment. The potential undesirable effects that may occur are:

- Reduction (hypovolaemia) or increase (hypervolaemia) in body fluid volume
- Reduction (hypotension) or increase (hypertension) in blood pressure
- Very low blood phosphate (hypophosphataemia)
- Disturbance in the alkali level in your blood (alkalosis)
- Feeling sick
- Vomiting
- Muscle cramps
- Bleeding disorder
- Infection
- Shortness of breath, irregular breathing (caused by air bubbles getting into the blood stream)
- Disturbance in the different salt levels in your blood (e.g. disturbance in sodium, potassium, calcium in your blood)
- Increase blood clotting.

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

HPRA Pharmacovigilance
Website: www.hpra.ie

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

5. How to store Accusol 35

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

Do not refrigerate or freeze. Do not use this medicine after the expiry date which is stated on the label and carton after 'Exp.' 'The expiry date refers to the last day of that month.

Your doctor will not use Accusol 35 if the solution is not clear or if the container is damaged.'

6. Contents of the pack and other information

Name of the Medicinal Product

Accusol 35, Solutions for haemofiltration, haemodialysis and haemodiafiltration.

The composition of the solution Accusol 35 is:

Ingredients	**Per 1000 ml Accusol 35**
Large chamber 'A'	
Calcium chloride dihydrate	0.343 g
Magnesium chloride hexahydrate	0.136 g
Sodium chloride	7.52 g
Small chamber 'B'	
Sodium bicarbonate	13.4 g

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

Ionic Composition of Final Solution is:

	Per 1000 ml Accusol 35
Calcium (Ca^{++})	1.75 mmol
Magnesium (Mg^{++})	0.5 mmol
Sodium (Na^{+})	140 mmol
Chloride (Cl^{-})	109.3 mmol
Bicarbonate (HCO_3^{-})	35 mmol
Theoretical osmolarity	**287 mOsm/l**

The other ingredients are: water for injections, hydrochloric acid, sodium hydroxide and disodium phosphate dihydrate.

What Accusol 35 looks like and contents of the pack

Accusol 35 is supplied in a carton box containing two units of 5 litre two-chamber non-PVC bags.

Each bag is over-wrapped in its overpouch.

The solution in the bag is clear and colourless.

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Manufacturers:

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The following information is intended for medical or Healthcare professionals only

INFORMATION FOR THE HEALTH PROFESSIONAL

Accusol 35, Solution for haemofiltration, haemodialysis and haemodiafiltration

1. NAME OF THE MEDICINAL PRODUCT

Accusol 35
Solution 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	7.52 g
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	2.94 g

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
Chloride (Cl^{-})	109.3 mmol

Bicarbonate (HCO_3^-)	35 mmol
Theoretical osmolarity	**287 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

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 is primarily intended for use in patients with hyperkalaemia.

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 extra corporeal 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 5.5.

4.3 Contraindications

Solution dependent contraindications
- Hypokalaemia, if no simultaneous adapted potassium supplementation.
- 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,
- Accusol 35 is potassium-free. Kalaemia must be monitored regularly before and during treatment. If hypokalaemia is present or starts to develop, supplementation of potassium and/or changing to a substitution solution with higher potassium concentration may be required. If hyperkalaemia starts to develop an increase in the filtration rate may be indicated as well as usual measures of intensive care medicine,
- Accusol 35 is glucose-free. 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 interaction

When prescribing Accusol 35, 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 of 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
Website: www.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. PHARMACEUTICAL PARTICULARS

5.1 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in Section 5.5

5.2 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.

5.3 Special precautions for storage

Do not refrigerate or freeze.

5.4 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.

5.5 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 (interchamber 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 SafetyMoon 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.

6. MARKETING AUTHORISATION HOLDER

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7. MARKETING AUTHORISATION NUMBER(S)

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