multiBic® 2 mmol/L potassium solution for haemodialysis/haemofiltration

KOREA
Package Leaflet

멀티빅 2 칼륨액 5 L

전문의약품

[원료약품 및 분량]

	각 1L 중	분 량
A 액	염화칼슘이수화물 (EP)	4.410 g
	염화마그네슘육수화물 (EP)	2.033 g
	염화칼륨 (EP)	2.982 g
	포도당수화물 (EP)	22.00 g
	(무수포도당으로서)	(20.00 g)
	주사용수 , 염산 25%	
B 액	염화나트륨 (EP)	6.453 g
	탄산수소나트륨 (EP)	3.104 g
	주사용수 , 이산화탄소	
혼합액	나트륨	140.0 mmol
	칼륨	2.0 mmol
	칼슘	1.50 mmol
	마그네슘	0.50 mmol
	염소	111.0 mmol
	탄산수소염	35.0 mmol
	포도당	5.55 mmol

〔 성상 〕 투명한 플라스틱 백에 든 무색 투명한 액상 제제

〔 효능효과 〕
- 급성 신부전 환자의 연속 혈액여과 및 혈액투석여과시 체액대용액으로 사용
- 급성 신부전환자의 연속 혈액투석 시 투석액으로 사용 - 이 액은 특히 고칼륨혈증의 가능성이 있는 환자에게 적응된다 .

〔 용법용량 〕

1. 용법

환자의 체액평형상태 , 목적하는 체액평형상태 및 환자 혈액 중 여과되는 양에 따라 투여량이 결정되며 , 의사의 지시에 따라서 투여되어야 한다 .

1) 일반적으로 , 혈액여과 및 혈액투석여과시 체액대용액 유속은 다음과 같다 .
   성 인 : 500~1500mL/h 소 아 : 15~20mL/kg/h
2) 일반적으로 , 연속 혈액투석시 투석액 유속은 다음과 같다 .
   성 인 : 500~2000mL/h 소 아 : 15~20mL/kg/h
   고령자의 경우는 성인의 투여법에 따르되 , 주입속도는 환자의 혈액학적 상태에 따라 결정된다 .

2. 최종 전해질 농도 (단위 : mEq/L)

Na^+	K^+	Ca^{2+}	Mg^{2+}	Cl^-	HCO_3^-
140	2.0	3.0	1.0	111	35

포도당 : 1.0g/L

3. 투여방법

체액대용액으로 사용되는 경우 , 여과기 통과전 (predilution) 또는 후 (postdilution) 에 혈액회로에 투여한다 .

4. 사용방법

1) 겉 포장지를 제거하고 용액이 든 백을 잘 살핀다 . 운반 중 손상되어 박테리아나 곰팡이의 오염을 초래할 수 있으므로 사용 직전에 겉 포장지를 제거하고 용액이 든 백의 밀봉 , 접합부 , 코너를 살펴 용액이 무색투명하고 밀봉이 완전할 경우에만 사용한다 .
2) 사용 직전에 두 분획을 섞어야 하며 , 혼합 후 연결 부위가 완전히 열렸는지 확인하고 용기가 새지 않는지도 확인한다 .
3) 처방된 약물은 두 분획이 완전히 열리고 , 완전히 혼합된 후에만 추가 되어야 한다 .
4) 혼합액은 즉시 사용하여야 하며 , 최대 48 시간 이내에 사용하여야 한다 . 1 회 사용에 한하며 , 남은 용액은 버린다 .

〔 사용상의 주의사항 〕

1. 다음 환자에는 투여하지 말 것
   1) 대사성 알칼리증 환자
   2) 저칼륨혈증 환자
2. 이상반응
   1) 투석치료와 관련하여 구역 , 구토 , 근경련 , 저혈압 등이 일어날 수 있다 .
   2) 전해질 불균형 , 저인산혈증 , 고혈당증 , 대사성 알칼리증이 일어날 수 있다 .
   3) 과량 사용은 울혈성 심부전과 전해질 불균형을 초래할 수 있다 .
3. 일반적 주의
   1) 치료 중 환자의 혈액학적 상태 , 전해질 및 산 - 염기 평형은 치료기간 내내 주의 깊게 관찰해야 한다 .
   2) 가장 적합한 칼륨 농도를 정확하게 선택하기 위해 칼륨 농도의 모니터링이 수반되어야 하며 필요시 칼륨을 공급한다 . 또한 혈중 무기 인산 농도를 관찰하여 저인산혈증일 경우에는 무기인산제제를 투여한다 .
4. 상호작용
   1) 치료하는 동안 여과 / 투석이 가능한 약물의 혈중 농도가 감소될 것이므로 필요하면 상응하는 교정요법을 설정한다 .
   2) 비타민 D 제제나 칼슘함유 제제는 고칼슘혈증을 일으킬 수 있다 .
5. 임부 및 수유부에 대한 투여

임부 및 수유부에 대한 투여는 치료 상의 유익성이 위험성을 상회한다고 판단되는 경우에만 투여한다 .

6. 적응상의 주의
   1) 사용시에는 체온 (37℃) 정도의 온도로 한다 .
      : 본 용액은 주입 전 적당한 기구를 사용하여 체온 정도로 데워져야 하며 실온 이하의 환경에서는 주입되어서는 안 된다 . 용액을 데울 때에는 주의 깊게 관찰되어야 하며 용액이 투명한지 입자가 없는지 확인하여야 한다 . 다른 처방이 없으면 주입 직전에 데워야 하며 정확한 온도는 의사의 지시에 따른다 . 투석액을 데우는데 승인된 기구를 사용하여 데워야 하며 전용제품 사용을 권고한다 . 전자레인지를 사용하여 데우면 부분적으로 과열될 수 있으므로 금지한다 .
   2) 혼합 전에 제품이 투명한지 , 모든 봉합이 그대로인지 확인한다 .
   3) 혈액여과 / 혈액투석여과 / 연속혈액투석에 적합한 최종 용액을 얻기 위해 반드시 사용전에 전해질 용액을 환충액과 혼합하여야 하며 혼합액이 투명하지 않는 경우 , 사용하지 않는다 .
   4) 라인세트의 연결과 분리시 무균조작을 실시하여야 한다 .
   5) 본 용액으로 치료하는 동안 드물게 튜브에서 특히 펌프의 데두는 곳 가까이에서 환색의 탄산칼슘 침전물이 발견될 수 있다 . 탄산칼슘 침전물은 특히 펌프 주입구 주변의 용액 온도가 25℃ 이상이 되었을 때 일어날 수 있다 . 그러므로 튜브내의 용액은 튜브 시스템이 투명하고 침전물이 없음을 확인하기 위해 30 분마다 확인하여야 한다 . 침전물은 임상 치료시간이 상당히 늘어질 수 있다 . 약약 침전물이 발견되면 즉시 치료를 중단하고 본 용액과 라인을 교체하여야 하며 환자를 면밀히 살펴야 한다 . 혼합액은 25℃이하에서 보관하여야 하며 25℃ 이상에서 보관되었거나 48 시간 (이 약을 이용하여 치료하는 시간 포함) 을 넘긴 혼합액은 사용하지 않는다 .
7. 기타

운전이나 기계사용 능력에 대한 영향은 보고된 바 없다 .

〔 포장단위 〕 5,000mL x 2 bags/ box

〔 저장방법 〕 밀봉용기 , 4~30℃에서 보관

* 본 의약품은 엄격한 품질관리를 필한 제품입니다 . 만약 구입시 사용기한이 경과되었거나 , 변질 변패 또는 오손된 제품이 발견될 경우에는 교환하여 드립니다 . (연락처 : 02-2112-8800.)

* 자세한 품목 허가사항은 식품의약품안전처 온라인의약도서관 (http://drug.mfds.go.kr) ' 의약품등 정보 ' 란에서 확인하실 수 있습니다 .

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〈 최종 개정 연월일 〉 2017 년 12 월 3 일

FRESENIUS MEDICAL CARE
THE RENAL COMPANY

multiBic® 2 mmol/L potassium solution for haemodialysis/haemofiltration

MALAYSIA
Package Insert

1. Product Name

multiBic® 2 mmol/L potassium Solution for haemodialysis/haemofiltration

2. Name and Strength of Active Ingredient(s)

Active substance:

1000mL of the ready-to-use solution for haemodialysis/haemofiltration contain:

	multiBic® 2 mmol/L potassium
Sodium chloride	6.136 g
Potassium chloride	0.1491 g
Sodium hydrogen carbonate	2.940 g
Calcium chloride dihydrate	0.2205 g
Magnesium chloride hexahydrate	0.1017 g
Glucose monohydrate	1.100 g
(Glucose)	(1.000 g)

	multiBic® 2 mmol/L potassium
K^+	2.0 mmol/L
Na^+	140 mmol/l
Ca^{2+}	1.5 mmol/l
Mg^{2+}	0.50 mmol/l
Cl^-	111 mmol/l
HCO_3^-	35 mmol/l
Glucose	5.55 mmol/l

The other ingredients are water for injections, hydrochloric acid 25%, carbon dioxide, and Sodium dihydrogen phosphate dihydrate.

3. Product Description

multiBic® 2 mmol/L potassium is a solution for haemodialysis/haemofiltration. The solution is clear and colourless.

Theoretical osmolarity: 296 mosm/l pH≈7.4

4. Pharmacodynamics/ Pharmacokinetics

4.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Haemofiltrates

ATC code: B05Z B

Mechanism of action

Basic principles of haemodialysis, haemofiltration and haemodiafiltration:

During haemofiltration water and solutes such as uremic toxins, electrolytes, and bicarbonate are removed from the blood by ultrafiltration. The ultrafiltrate is replaced by a solution for haemofiltration, with a balanced electrolyte and buffer composition.

During haemodialysis, water and solutes such as uremic toxins, electrolytes, bicarbonate and other small molecules are exchanged between the patient's blood and the solution for haemodialysis by diffusion. The direction and the magnitude of the diffusion process depend on the relevant concentration gradients between the blood and the solution for haemodialysis.

In haemodiafiltration, the underlying principles of haemofiltration and haemodialysis are combined.

This medicinal product is a bicarbonate-buffered solution for intravenous administration or for use as haemodialysis solution for the balancing of water and electrolyte removal during continuous renal replacement therapies which are applied, e.g. in the treatment of acute kidney injury.

The electrolytes $Na+$, $K+$, Mg^{2+}, Ca^{2+}, Cl^-, and bicarbonate are essential for the maintenance and correction of fluids and electrolyte homeostasis (blood volume, osmotic equilibrium, acid-base balance).

Paediatric population:

There is no clinical experience on the use of this product in children. This medicinal product is not recommended for use in children until further data become available (see sections 7 and 9).

4.2 Pharmacokinetic Properties

This medicinal product must only be administered intravenously or used as haemodialysis solution.

Distribution/ Biotransformation/ Elimination:

The distribution of electrolytes and bicarbonate is regulated in accordance with requirements and the metabolic status and residual renal function. The active substances of this medicinal product are not metabolised except for glucose. The elimination of water and electrolytes depends on cellular requirements, the metabolic status, the residual renal function, and on other routes of fluid losses (e.g., gut, lung, and skin).

5. Indication

multiBic® 2 mmol/L potassium is indicated for intravenous use as substitution solution in haemofiltration and haemodiafiltration, and as dialysis solution in haemodialysis and haemodiafiltration.

For use in patients

- with acute kidney injury requiring continuous renal replacement therapy: continuous haemodialysis, haemofiltration or haemodiafiltration treatments.
- with chronic kidney disease in whom a transient treatment is indicated, e.g. during the stay on an intensive care unit.
- when continuous renal replacement therapy is indicated as part of the treatment of an intoxication with water soluble, filterable/dialyzable toxins.

multiBic® 2 mmol/L potassium is indicated in adults.

6. Recommended Dose

Continuous renal replacement therapy including the prescription of this medicinal product should be performed under the direction of a physician with experience in these treatments.

7. Mode of Administration

In acute kidney injury, a continuous treatment with a dose of 2000 ml/h multiBic® 2 mmol/L potassium is appropriate in adults with a body weight of 70 kg to remove metabolic waste products depending on the metabolic status of the patient. The dose should be adapted to the body size of the patient.

In patients with chronic kidney disease, unless clinically indicated otherwise, the dose of multiBic® 2 mmol/L potassium should be at least one third of the body weight per session with three sessions applied per week. Increasing the volume applied per week or distributing this weekly volume to more than 3 treatments per week can be required.

The dose and the duration of haemodialysis, haemofiltration or haemodiafiltration necessary in treatment of acute states of intoxication depends on the toxin and its concentration and the severity of clinical symptoms and has to be clinically decided on the individual patient's condition.

A maximum dose of 75 litre per day is recommended.

Paediatric population

The safety and efficacy of multiBic® 2 mmol/L potassium in children have not yet been established (see sections 9 and 4.1).

Method of administration

For intravenous use and haemodialysis.

Do not use unless the ready-to-use solution is clear and colourless and the bag and connectors are undamaged.

For single use only. Any unused solution must be discarded.

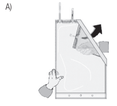
Must be used by means of metering pumps.

The following information is intended for medical or healthcare professionals only.

Instructions for use

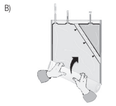
1. Removal of the protective foil and careful inspection of the bag
   The protective foil should only be removed immediately before administration.
   Plastic containers may occasionally be damaged during transport from the manufacturer to the clinic or within the clinic itself. This can lead to contamination and microbiological or fungal growth in the solutions. Therefore, careful visual inspection of the bag and the solutions before mixing is necessary. Particular attention should be paid to even the slightest damage to the closure, the welded seam and the corners of the bag in view of a possible contamination.
2. Mixing of the two compartments
   The two-compartment-bag : the bicarbonate and the electrolytes including glucose compartments - are mixed immediately before use to obtain a ready-for-use solution.

A)



Unfold the small compartment.

B)



Roll up the solution bag starting from the corner opposite the small compartment…

C)

… until the peel seam between both compartments has opened along its entire length and the solutions from both compartments are mixed.

After mixing both compartments, it must be checked, that the peel seam is completely open, that the mixed solution is clear and colourless and that the bag is not leaking.

3. Application of the ready-to-use solution
   The ready-to-use solution must be used immediately, but within a maximum of 48 hours after mixing.
   Any admixture to the ready-to-use solution must only be done after the ready-to-use solution has been thoroughly mixed. After such an admixture, the ready-to-use solution should again be thoroughly mixed prior to use.
   Admixtures of sodium chloride solution (concentration between 3% and 30% sodium chloride; up to 250 mmol sodium chloride per 5 litre multiBic solution) and water for injection (up to 1250 ml per 5 litre multiBic solution) are compatible with this medicinal product.
   If not otherwise prescribed, the ready-to-use solution should be warmed immediately before use to 36.5°C – 38.0°C. The exact temperature must be selected depending on clinical requirements and the technical equipment used.
   No special requirements for disposal. This medicinal product must not be mixed with other medicinal products except those mentioned above.

8. Contraindication

Solution related contraindications

- Hypersensitivity to the active substances or to any of the excipients listed in section 2
- Hypokalaemia
- Metabolic alkalosis

Contraindications for use of the technical procedure itself

- Inadequate blood flow from vascular access.
- If there is a high risk of haemorrhage on account of systemic anticoagulation.

9. Warnings and Precautions

Use only after mixing of the two solutions.

multiBic® 2 mmol/L potassium should be warmed prior to use with appropriate equipment to approximately body temperature and must not be used under any circumstances below room temperature.

The warming of the ready-to-use solution to approximately body temperature must be carefully controlled verifying that the ready-to-use solution is clear and without particles.

During application of the ready-to-use solution, white calcium carbonate precipitation has been observed in the tubing lines in rare cases, particularly close to the pump unit and the heating unit warming the ready-to-use solution.

Precipitations particularly can occur if the temperature of the ready-to-use solution at the inlet of the pump unit is already higher than 30°C.

Therefore, the ready-to-use solution in the tubing lines must be closely visually inspected every 30 min during continuous renal replacement therapy in order to ensure, that the solution in the tubing system is clear and free from precipitate. Precipitations may occur also with substantial delay after start of treatment.

If precipitate is observed, the ready-to-use solution and the tubing lines used for continuous renal replacement therapy must be replaced immediately and the patient carefully monitored.

The serum potassium concentration must be checked regularly before and during continuous renal replacement therapy. The potassium status of the patient and its trend during the treatment must be considered:

In case of hypokalaemia supplementation of potassium and / or changing to a solution for haemodialysis/haemofiltration with higher potassium concentration may be required.

In case of hyperkalaemia an increase in the applied dose and / or change to a solution for haemodialysis/haemofiltration with a lower potassium concentration may be indicated as well as usual measures of intensive care medicine.

The serum sodium concentration must be checked regularly before and during use of this solution for haemodialysis/haemofiltration to control risks related to hypo/ hypernatraemia. The solution for haemodialysis/haemofiltration may be diluted with an adequate amount of water for injections or concentrated sodium chloride solution may be added if required. The speed of desired normalisation must then be carefully planned to avoid adverse reactions due to rapid changes in serum sodium concentration.

In addition, the following parameters must be monitored before and during continuous renal replacement therapy: Serum calcium, serum magnesium, serum phosphate, serum glucose, acid-base status, levels of urea and creatinine, body weight and fluid balance (for the early recognition of hyper- and dehydration).

Clinically important substances may be removed with the haemodialysis, haemofiltration and haemodiafiltration treatment and are not supplemented with this medicinal product. This removal of important nutrients must be compensated by adequate nutrition, nutritional supplements, or an adapted parenteral nutrition.

Paediatric population

There is no clinical experience on the use of this product in children. This medicinal product is not recommended for use in children until further data become available (see sections 7 and 4.1).

10. Interactions With Other Medicaments

No interaction studies have been performed.

The correct dose of multiBic® 2 mmol/L potassium and strict monitoring of clinical chemistry parameters and vital signs will avoid risks related to interactions with other medicinal products.

The following interactions are conceivable:

- Toxic effects of digitalis may be masked by hyperkalaemia, hypermagnesaemia and hypocalcaemia. The correction of these electrolytes by continuous renal replacement therapy may precipitate signs and symptoms of digitalis toxicity, e.g. cardiac arrhythmia.
- Electrolyte substitutions, parenteral nutrition and other infusions usually given in intensive care medicine interact with the serum composition and the fluid status of the patient. This must be considered during application of continuous renal replacement therapy.
- Continuous renal replacement therapy may reduce the blood concentration of drugs, especially of drugs with a low protein binding capacity, with a small distribution volume, with a molecular weight below the cut-off of the haemofilter and of medicinal products adsorbed to the haemofilter. An appropriate revision of the dose of such medicinal products may be required.

11. Pregnancy and Lactation

There are no or limited amount of data from the use of multiBic® 2 mmol/L potassium in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. multiBic® 2 mmol/L potassium should not be used during pregnancy unless the clinical condition of the woman requires continuous renal replacement therapy.

There is insufficient information on the excretion of multiBic® 2 mmol/L potassium active substances/metabolites in human milk.

Breastfeeding is not recommended during treatment with multiBic® 2 mmol/L potassium.

12. Undesirable Effects

Adverse reactions may result from the treatment mode itself or may be induced by this medicinal product.

Gastrointestinal disorders - nausea, vomiting

Vascular disorders - hypertension, hypotension

Musculoskeletal and connective tissue disorders - muscle cramps

The following adverse reaction can be anticipated for the treatment mode:

Metabolism and nutrition disorders - hyper- or hypohydration, electrolyte disturbances (e.g., hypokalaemia), hypophosphataemia, hyperglycaemia, and metabolic alkalosis.

The exact frequency of such events is not known (cannot be estimated from the available data).

13. Overdose and treatment

After use of recommended doses no reports of emergency situations have arisen; moreover, the administration of this medicinal product can be discontinued at any time. If fluid balance is not accurately calculated and monitored, hyperhydration or dehydration may occur, with the resultant associated circulatory reactions. These may be manifest through changes in blood pressure, central venous pressure, heart rate, and pulmonary arterial pressure. In cases of hyperhydration congestive cardiac failure and/or pulmonary congestion may be induced.

In cases of hyperhydration, net fluid removal should be increased on the device used for continuous renal replacement therapy. In cases of marked dehydration, net fluid removal by the device used for continuous renal replacement therapy should be decreased or discontinued; alternatively, fluid resuscitation can be applied to restore the hydration status.

If too large volume is applied, this may result in disturbances of electrolyte concentrations and the acid-base-balance, e. g. an overdose of bicarbonate may occur if an inappropriate large volume of the solution for haemodialysis/haemofiltration is infused / administered. This could possibly lead to metabolic alkalosis, decrease of ionized calcium, or tetany.

14. Storage Condition

Store below 30°C. Do not store below 4°C. Keep out of reach and sight of children.

Shelf life: 24 months

Chemical and physical in-use stability of the ready-to-use solution has been demonstrated for 48 hours at 30 °C. It is not recommended to store the ready-to-use solution longer than 48 hours including duration of treatment or at a temperature higher than 30 °C prior to the inlet of the pump unit.

From a microbiological point of view, once connected to the haemodialysis, haemofiltration or haemodiafiltration circuit, and as hydrogen carbonate is present, the product shall be used immediately.

15. Dosage Forms and packaging available

multiBic® 2 mmol/L potassium is delivered in a double chamber bag (two-compartment). Mixing of both solutions by opening the seam between the two chambers result in the ready-to –use solution for haemofiltration.

Each bag contains 5000ml, solution in total.

Pack size: 2 bags of 5000mL

16. Name and Address of Manufacturer/Marketing Authorization Holder/ Product Registration Holder

Marketing Authorization Holder
Fresenius Medical Care Deutschland GmbH
Else-Kröner-Straße 1
61352 Bad Homburg v.d.H
Germany

Manufacturer
Fresenius Medical Care Deutschland GmbH
Frankfurter Straße 6-8,
66606 St. Wendel, Germany

Product Registration Holder
Fresenius Medical Care Malaysia Sdn.Bhd.,
2nd Floor, Axis Technology Centre,
Lot 13, Jalan 51A/225, 46100 Petaling Jaya, Selangor, Malaysia.

17. Date of Revision of Package Insert

The insert was last revised in September 2017

0875372/01

FRESENIUS MEDICAL CARE
THE RENAL COMPANY

multiBic® 2 mmol/L potassium solution for haemodialysis/haemofiltration

HONG KONG
Package Leaflet

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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What multiBic® 2 mmol/l potassium is and what it is used for

multiBic® 2 mmol/l potassium is a continuous renal replacement therapy solution for removal of waste products from the body in people with kidney disease. It is used in patients with kidney injury and also for the treatment of poisoning. The type of solution you are given depends on the amount of potassium (a salt) in your blood. Your doctor will check your potassium levels regularly.

2. What you need to know before you use multiBic® 2 mmol/l potassium

Do not use multiBic® 2 mmol/l potassium if
- you are allergic to any of the active substances or any of the other ingredients of this medicine (listed in section 6)
- you have hypokalaemia (your potassium level is very low)
- you have metabolic alkalosis (a condition where there is too much bicarbonate in the blood)
- you cannot achieve a sufficient blood flow through the haemofilter (filter used in the blood filtration)
- you have a high risk of bleeding related to medications required to prevent clotting in the haemofilter

Warnings and precautions

Talk to your doctor before using multiBic® 2 mmol/l potassium.
- Must be used only after mixing the two solutions in the double chamber (two-compartment) bag.
- Must not be used under any circumstances below room temperature.
- The tubing lines used to apply the ready-to-use solution should be inspected every 30 minutes. If precipitate (solid matter) is observed within these tubing lines, bag and tubing lines must be replaced immediately and the patient carefully monitored.
- Your doctor will check your hydration status (the amount of water in your body), the levels of potassium, sodium, other salts, certain waste products, and your blood sugar levels. Your doctor also might advise you about your diet.

Children

Use of multiBic® 2 mmol/l potassium has not been established in children.

Other medicines

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

Following interactions are conceivable:
- toxic effects of digitalis (medicine for treatment of heart disease)
- electrolyte substitutions, parenteral nutrition (intravenous feeding) and other infusions treatment. Their effect on blood serum concentration and fluid status must be considered when using this therapy
- This therapy may reduce the blood concentration of medicinal products. Dose adjustment may be required.

Pregnancy and breast-feeding

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 starting treatment with this medicine.

There are no or limited amount of data on the use of multiBic® 2 mmol/l potassium during pregnancy and breast-feeding.

This medicine should only be used during pregnancy if your doctor considers treatment necessary.

Breast-feeding is not recommended during treatment with multiBic® 2 mmol/l potassium.

3 How to use multiBic® 2 mmol/l potassium

multiBic® 2 mmol/l potassium will be given in a hospital or clinic. Your doctor will know how to use this medicine.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The side effects of multiBic® 2 mmol/l potassium include:
- nausea (feeling sick)
- vomiting (being sick)
- muscle cramps
- changes in blood pressure

Some side effects might be caused by too much or too little fluid. These are:
- shortness of breath
- swelling of the ankles and legs
- dehydration (e.g. dizziness, muscle cramps, feeling thirsty)
- blood disorders (e.g. abnormal salt concentrations in your blood)

The exact frequency of such events is not known (cannot be estimated from the available data).

Reporting of side effects

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

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

5. How to store multiBic® 2 mmol/l potassium

Your doctor knows how to store multiBic® 2 mmol/l potassium.

Store below 30°C. Do not store below 4°C.

請將產品儲存於溫度攝氏 30°C 以下及 4°C 以上。

Keep out of the reach and sight of children.

6. Content of the pack and other information

What multiBic® 2 mmol/l potassium contains
- The active substances are potassium chloride, sodium chloride, sodium hydrogen carbonate, calcium chloride dihydrate, magnesium chloride hexahydrate, glucose monohydrate.
- The other ingredients are water for injections, hydrochloric acid 25 %, carbon dioxide and sodium dihydrogen phosphate dihydrate.

What multiBic® 2 mmol/l potassium looks like and contents of the pack

multiBic® 2 mmol/l potassium is delivered in a double chamber bag (two-compartments containing different solutions). Mixing of the solutions in both compartments results in the ready-to-use solution.

Each bag contains 5000 ml solution in total. The ready-to-use solution is clear and colourless.

Each bag is equipped with a HF-connector, a Luer-lock-connector and an injection port, and is covered by a protective foil.

Pack size:
2 bags of 5000 ml HK-XXXXX

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Fresenius Medical Care Deutschland GmbH, Else-Kröner-Straße 1, 61352 Bad Homburg v.d.H., Germany

Manufacturer

Fresenius Medical Care Deutschland GmbH, Frankfurter Straße 6-8, 66606 St. Wendel, Germany

This leaflet was last revised in July 2017.

Information for healthcare professionals only see end of this package leaflet.

The following information is intended for healthcare professionals only:

1000 ml of the ready-to-use solution contain:

Potassium chloride	0.1491 g
Sodium chloride	6.136 g
Sodium hydrogen carbonate	2.940 g
Calcium chloride dihydrate	0.2205 g
Magnesium chloride hexahydrate	0.1017 g
Glucose monohydrate	1.100 g
(Glucose)	(1.000 g)

K^+	2.0 mmol/l
Na^+	140 mmol/l
Ca^{2+}	1.5 mmol/l
Mg^{2+}	0.50 mmol/l
Cl^-	111 mmol/l
HCO_3^-	35 mmol/l
Glucose	5.55 mmol/l

pH ≈ 7.4

Theoretical osmolarity (Theor. osmolar.) 296 mOsm/l

Do not use unless the ready-to-use solution is clear and colourless and the bag and connectors are undamaged.

For single use only. Any unused solution must be discarded.

Must be used by means of metering pumps.

Instructions for use

1. Removal of the protective foil and careful inspection of the bag containing the haemofiltration solution
   The protective foil should only be removed immediately before using the solution.
   Plastic containers may occasionally be damaged during transport from the manufacturer to the dialysis clinic or hospital clinic or within the clinic itself. This can lead to contamination and the growth of bacteria or a fungus in the solution for haemofiltration. Therefore careful inspection of the bag and of the solution before use is necessary. Particular attention should be paid to even the slightest damage to the closure of the bag, the welded seam and the corners of the bag. The solution should only be used if bag and colourless and if the container (the bag) and connectors are undamaged and are intact.
   In case of doubt the doctor should decide whether the haemofiltration solution should be used or not.
2. Mixing of the solutions in the double chamber bag.
   The two solutions should be mixed immediately before use to produce a solution ready-to-use. The solution is clear and colourless.

A)

Unfold the small compartment.

B)

Roll up the solution bag starting from the corner opposite the small compartment …

C)

… until the peel seam between both compartments has opened along its entire length and the solutions from both compartments are mixed.

After mixing both compartments, it must be checked, that the peel seam is completely open, that the solution is clear and colourless and that the container is not leaking.

3. Ready-to-use solution
   If prescribed, medicinal products (drugs) may be added to the ready-to-use haemofiltration solution. This should only be carried out after the seam between the two chambers has been fully opened and the two solutions have been thoroughly mixed. The addition of any drugs to the haemofiltration solution would only be carried out on the doctor's advice and care must be taken not to introduce any contamination into the bag. After a drug has been added to the haemofiltration solution, the solution should be thoroughly mixed again before administration of the solution to the patient. The bags should be labeled with details of the name and amount of drug, together with the time and date.
   The ready-to-use solution should be used immediately, not stored above +25°C and must be used within a maximum of 48 hours after mixing. Chemical and physical in-use stability of the ready-to-use solution has been demonstrated for 48 hours at 25°C. Other in-use storage times and conditions prior to use (longer than 48 hours including the duration of the treatment, higher than 25°C prior to the inlet of the pump unit) are the responsibility of the user.From a microbiological point of view, once connected to the haemofiltration circuit, and as hydrogen carbonate is present, the product shall be used immediately. Other in-use storage times and conditions are the responsibility of the user.
   The haemofiltration solution should be warmed prior to infusion with appropriate equipment to approximately body temperature and must not be infused under any circumstances below room temperature.
   The warming of this solution to approximately body temperature must be carefully controlled verifying that the solution is clear and without particles. If not otherwise prescribed, the ready-to-use solution for haemofiltration should be warmed immediately before infusion into the patient to 36.5°C - 38°C. The exact temperature must be selected on the doctor's advice depending on the clinical need. Only devices approved for warming haemofiltration solutions must be used. The use of a dedicated device for haemofiltration treatments which will also warm the solutions for haemofiltration prior to infusion is recommended. Microwave ovens must not be used to warm multiBic® 2 mmol/L potassium due to the possibility of local overheating.
   During application of multiBic in CRRT, white calcium carbonate precipitation has been observed in the tubing lines in rare cases, particularly close to the pump unit and the heating unit warming multiBic. Precipitations particularly can occur if the temperature of the multiBic solution at the inlet of the pump unit is already higher than 25°C. Therefore, the multiBic solution in the tubing lines should be closely visually inspected every 30 min during CRRT in order to ensure, that the solution in the tubing system is clear and free from precipitate. Precipitations may occur also with substantial delay after start of treatment. If precipitate is observed, multiBic solution and CRRT tubing lines must be replaced immediately and the patient carefully monitored.
   The haemofiltration solution is for single use only; any unused solution and any damaged containers should be discarded.

FRESENIUS MEDICAL CARE
THE RENAL COMPANY

multiBic® 2 mmol/L potassium solution for haemodialysis/haemofiltration

INDIA
Package Leaflet

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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What multiBic® 2 mmol/l potassium is and what it is used for

multiBic® 2 mmol/l potassium is a continuous renal replacement therapy solution for removal of waste products from the body in people with kidney disease. It is used in patients with kidney injury and also for the treatment of poisoning. The type of solution you are given depends on the amount of potassium (a salt) in your blood. Your doctor will check your potassium levels regularly.

2. What you need to know before you use multiBic® 2 mmol/l potassium

Do not use multiBic® 2 mmol/l potassium if
- you are allergic to any of the active substances or any of the other ingredients of this medicine (listed in section 6)
- you have hypokalaemia (your potassium level is very low)
- you have metabolic alkalosis (a condition where there is too much bicarbonate in the blood)
- you cannot achieve a sufficient blood flow through the haemofilter (filter used in the blood filtration)
- you have a high risk of bleeding related to medications required to prevent clotting in the haemofilter

Warnings and precautions

Talk to your doctor before using multiBic® 2 mmol/l potassium.
- Must be used only after mixing the two solutions in the double chamber (two-compartment) bag.
- Must not be used under any circumstances below room temperature.
- The tubing lines used to apply the ready-to-use solution should be inspected every 30 minutes. If precipitate (solid matter) is observed within these tubing lines, bag and tubing lines must be replaced immediately and the patient carefully monitored.
- Your doctor will check your hydration status (the amount of water in your body), the levels of potassium, sodium, other salts, certain waste products, and your blood sugar levels. Your doctor also might advise you about your diet.

Children

Use of multiBic® 2 mmol/l potassium has not been established in children.

Other medicines

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

Following interactions are conceivable:
- toxic effects of digitalis (medicine for treatment of heart disease)
- electrolyte substitutions, parenteral nutrition (intravenous feeding) and other infusions treatment. Their effect on blood serum concentration and fluid status must be considered when using this therapy
- This therapy may reduce the blood concentration of medicinal products. Dose adjustment may be required.

Pregnancy and breast-feeding

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 starting treatment with this medicine.

There are no or limited amount of data on the use of multiBic® 2 mmol/l potassium during pregnancy and breast-feeding.

This medicine should only be used during pregnancy if your doctor considers treatment necessary.

Breast-feeding is not recommended during treatment with multiBic® 2 mmol/l potassium.

3 How to use multiBic® 2 mmol/l potassium

multiBic® 2 mmol/l potassium will be given in a hospital or clinic. Your doctor will know how to use this medicine.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The side effects of multiBic® 2 mmol/l potassium include:
- nausea (feeling sick)
- vomiting (being sick)
- muscle cramps
- changes in blood pressure

Some side effects might be caused by too much or too little fluid. These are:
- shortness of breath
- swelling of the ankles and legs
- dehydration (e.g. dizziness, muscle cramps, feeling thirsty)
- blood disorders (e.g. abnormal salt concentrations in your blood)

The exact frequency of such events is not known (cannot be estimated from the available data).

Reporting of side effects

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

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

5. How to store multiBic® 2 mmol/l potassium

Your doctor knows how to store multiBic® 2 mmol/L potassium.

Store below 30°C. Do not store below 4°C.

6. Content of the pack and other information

What multiBic® 2 mmol/l potassium contains
- The active substances are potassium chloride, sodium chloride, sodium hydrogen carbonate, calcium chloride dihydrate, magnesium chloride hexahydrate, glucose monohydrate.
- The other ingredients are water for injections, hydrochloric acid 25 %, carbon dioxide and sodium dihydrogen phosphate dihydrate.

What multiBic® 2 mmol/l potassium looks like and contents of the pack

multiBic® 2 mmol/l potassium is delivered in a double chamber bag (two-compartments containing different solutions). Mixing of the solutions in both compartments results in the ready-to-use solution.

Each bag contains 5000 ml solution in total. The ready-to-use solution is clear and colourless.

Each bag is equipped with a HF-connector, a Luer-lock-connector and an injection port, and is covered by a protective foil.

Pack size:
2 bags of 5000 ml

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Fresenius Medical Care Deutschland GmbH, Else-Kröner-Straße 1, 61352 Bad Homburg v.d.H., Germany

Manufacturer

Fresenius Medical Care Deutschland GmbH, Frankfurter Straße 6-8, 66606 St. Wendel, Germany

Imported and Distributed by:

Fresenius Medical Care India Pvt. Ltd., B7 & B8, Middle Portion, SIPCOT Industrial Park, Irungattukottai, Sriperumbudur, Chennai, 602105, India

Customer Care Number: 18001209500

Email ID: customerservice.india@fmc-asia.com

This leaflet was last revised in July 2017.

Information for healthcare professionals only see end of this package leaflet.

The following information is intended for healthcare professionals only:

1000 ml of the ready-to-use solution contain:

Potassium chloride	0,1491 g
Sodium chloride	6.136 g
Sodium hydrogen carbonate	2.940 g
Calcium chloride dihydrate	0.2205 g
Magnesium chloride hexahydrate	0.1017 g
Glucose monohydrate	1.100 g
(Glucose)	(1.000 g)
K^+	2.0 mmol/l
Na^+	140 mmol/l
Ca^{2+}	1.5 mmol/l
Mg^{2+}	0.50 mmol/l
Cl^-	111 mmol/l
HCO_3^-	35 mmol/l
Glucose	5.55 mmol/l

pH ≈ 7.4

Theoretical osmolarity (Theor. osmolar.) 296 mOsm/l

Do not use unless the ready-to-use solution is clear and colourless and the bag and connectors are undamaged.

For single use only. Any unused solution must be discarded.

Must be used by means of metering pumps.

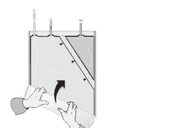
Instructions for use

1. Removal of the protective foil and careful inspection of the bag containing the haemofiltration solution
   The protective foil should only be removed immediately before using the solution.
   Plastic containers may occasionally be damaged during transport from the manufacturer to the dialysis clinic or hospital clinic or within the clinic itself. This can lead to contamination and the growth of bacteria or a fungus in the solution for haemofiltration. Therefore careful inspection of the bag and of the solution before use is necessary.
   Particular attention should be paid to even the slightest damage to the closure of the bag, the welded seam and the corners of the bag. The solution should only be used if clear and colourless and if the container (the bag) and connectors are undamaged and are intact.
   In case of doubt the doctor should decide whether the haemofiltration solution should be used or not.
2. Mixing of the solutions in the double chamber bag.
   The two solutions should be mixed immediately before use to produce a solution ready-to-use. The solution is clear and colourless.

A)

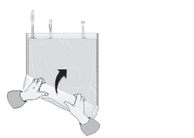
Unfold the small compartment.

B)



Roll up the solution bag starting from the corner opposite the small compartment ....

C)



... until the peel seam between both compartments has opened along its entire length and the solutions from both compartments are mixed.

After mixing both compartments, it must be checked, that the peel seam is completely open, that the solution is clear and colourless and that the container is not leaking.

3. Ready-to-use solution
   If prescribed, medicinal products (drugs) may be added to the readyto-use haemofiltration solution. This should only be carried out after the seam between the two chambers has been fully opened and the two solutions have been thoroughly mixed. The addition of any drugs to the haemofiltration solution would only be carried out on the doctor's advice and care must be taken not to introduce any contamination into the bag. After a drug has been added to the haemofiltration solution, the solution should be thoroughly mixed again before administration of the solution to the patient. The bags should be labeled with details of the name and amount of drug, together with the time and date.
   The ready-to-use solution shall be used immediately, not stored above +25°C and must be used within a maximum of 48 hours after mixing. Chemical and physical in-use stability of the ready-to-use solution has been demonstrated for 48 hours at 25°C. Other in-use storage times and conditions prior to use (longer than 48 hours including the duration of the treatment, higher than 25°C prior to the inlet of the pump unit) are the responsibility of the user.From a microbiological point of view, once connected to the haemofiltration circuit, and as hydrogen carbonate is present, the product shall be used immediately. Other in-use storage times and conditions are the responsibility of the user.
   The haemofiltration solution should be warmed prior to infusion with appropriate equipment to approximately body temperature and must not be infused under any circumstances below room temperature.
   The warming of this solution to approximately body temperature must be carefully controlled verifying that the solution is clear and without particles. If not otherwise prescribed, the ready-to-use solution for haemofiltration should be warmed immediately before infusion into the patient to 36.5°C - 38°C. The exact temperature must be selected on the doctor's advice depending on the clinical need. Only devices approved for warming haemofiltration solutions must be used. The use of a dedicated device for haemofiltration treatments which will also warm the solutions for haemofiltration prior to infusion is recommended. Microwave ovens must not be used to warm multiBic® 2 mmol/L potassium due to the possibility of local overheating.
   During application of multiBic in CRRT, white calcium carbonate precipitation has been observed in the tubing lines in rare cases, particularly close to the pump unit and the heating unit warming multiBic. Precipitations particularly can occur if the temperature of the multiBic solution at the inlet of the pump unit is already higher than 25°C. Therefore, the multiBic solution in the tubing lines should be closely visually inspected every 30 min during CRRT in order to ensure, that the solution in the tubing system is clear and free from precipitate. Precipitations may occur also with substantial delay after start of treatment. If precipitate is observed, multiBic solution and CRRT tubing lines must be replaced immediately and the patient carefully monitored.
   The haemofiltration solution is for single use only; any unused solution and any damaged containers should be discarded.

FRESENIUS MEDICAL CARE
THE RENAL COMPANY

Haemodialysis/haemofiltration solution

℞

PHILIPPINES
Package Leaflet

multiBic® 2 mmol/L potassium solution for haemodialysis/haemofiltration

1. Product Name

multiBic® 2 mmol/L potassium Solution for haemodialysis/haemofiltration

2. Name and Strength of Active Ingredient(s)

Active substance:
1000mL of the ready-to-use solution for haemodialysis/haemofiltration contain:

	multiBic® 2 mmol/L potassium
Sodium chloride	6.136 g
Potassium chloride	0.1491 g
Sodium hydrogen carbonate	2.940 g
Calcium chloride dihydrate	0.2205 g
Magnesium chloride hexahydrate	0.1017 g
Glucose monohydrate (Glucose)	1.100 g (1.000 g)

	multiBic® 2 mmol/L potassium
K^+	2.0 mmol/L
Na^+	140 mmol/l
Ca^{2+}	1.5 mmol/l
Mg^{2+}	0.50 mmol/l
Cl^-	111 mmol/l
HCO_3^-	35 mmol/l
Glucose	5.55 mmol/l

The other ingredients are water for injections, hydrochloric acid 25%, carbon dioxide, and Sodium dihydrogen phosphate dehydrate.

3. Product Description

multiBic® 2 mmol/L potassium is a solution for haemodialysis/haemofiltration. The solution is clear and colourless.
Theoretical osmolarity: 296 mosm/l pH≈7.4

4. Pharmacodynamics/ Pharmacokinetics

4.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Haemofiltrates
ATC code: B05Z B
Mechanism of action
Basic principles of haemodialysis, haemofiltration and haemodiafiltration:
During haemofiltration water and solutes such as uremic toxins, electrolytes, and bicarbonate are removed from the blood by ultrafiltration. The ultrafiltrate is replaced by a solution for haemofiltration, with a balanced electrolyte and buffer composition.
During haemodialysis, water and solutes such as uremic toxins, electrolytes, bicarbonate and other small molecules are exchanged between the patient's blood and the solution for haemodialysis by diffusion. The direction and the magnitude of the diffusion process depend on the relevant concentration gradients between the blood and the solution for haemodialysis.
In haemodiafiltration, the underlying principles of haemofiltration and haemodialysis are combined.
This medicinal product is a bicarbonate-buffered solution for intravenous administration or for use as haemodialysis solution for the balancing of water and electrolyte removal during continuous renal replacement therapies which are applied, e.g. in the treatment of acute kidney injury.
The electrolytes Na+, K+, Mg^{2+}, Ca^{2+}, Cl^-, and bicarbonate are essential for the maintenance and correction of fluids and electrolyte homoeostasis (blood volume, osmotic equilibrium, acid-base balance).
Paediatric population:
There is no clinical experience on the use of this product in children. This medicinal product is not recommended for use in children until further data become available (see sections 7 and 9).

4.2 Pharmacokinetic Properties

This medicinal product must only be administered intravenously or used as haemodialysis solution.
Distribution/ Biotransformation/ Elimination:
The distribution of electrolytes and bicarbonate is regulated in accordance with requirements and the metabolic status and residual renal function. The active substances of this medicinal product are not metabolised except for glucose.
The elimination of water and electrolytes depends on cellular requirements, the metabolic status, the residual renal function, and on other routes of fluid losses (e.g., gut, lung, and skin).

5. Indication

multiBic® 2 mmol/L potassium is indicated for intravenous use as substitution solution in haemofiltration and haemodiafiltration, and as dialysis solution in haemodialysis and haemodiafiltration.
For use in patients
- with acute kidney injury requiring continuous renal replacement therapy: continuous haemodialysis, haemofiltration or haemodiafiltration treatments.
- with chronic kidney disease in whom a transient treatment is indicated, e.g. during the stay on an intensive care unit.
- when continuous renal replacement therapy is indicated as part of the treatment of an intoxication with water soluble, filterable/dialyzable toxins.

multiBic® 2 mmol/L potassium is indicated in adults.

6. Recommended Dose

Continuous renal replacement therapy including the prescription of this medicinal product should be performed under the direction of a physician with experience in these treatments.

7. Mode of Administration

In acute kidney injury, a continuous treatment with a dose of 2000 ml/h multiBic® 2 mmol/L potassium is appropriate in adults with a body weight of 70 kg to remove metabolic waste products depending on the metabolic status of the patient. The dose should be adapted to the body size of the patient.
In patients with chronic kidney disease, unless clinically indicated otherwise, the dose of multiBic® 2 mmol/L potassium should be at least one third of the body weight per session with three sessions applied per week. Increasing the volume applied per week or distributing this weekly volume to more than 3 treatments per week can be required.
The dose and the duration of haemodialysis, haemofiltration or haemodiafiltration necessary in treatment of acute states of intoxication depends on the toxin and its concentration and the severity of clinical symptoms and has to be clinically decided on the individual patient condition.
A maximum dose of 75 litre per day is recommended.
Paediatric population
The safety and efficacy of multiBic® 2 mmol/L potassium in children have not yet been established (see sections 9 and 4.1).
Do not use unless the ready-to-use solution is clear and colourless and the bag and connectors are undamaged.
For single use only. Any unused solution must be discarded.
Must be used by means of metering pumps.
The following information is intended for medical or healthcare professionals only.

Instructions for use

1. Removal of the protective foil and careful inspection of the bag
   The protective foil should only be removed immediately before administration.
   Plastic containers may occasionally be damaged during transport from the manufacturer to the clinic or within the clinic itself. This can lead to contamination and microbiological or fungal growth in the solutions. Therefore, careful visual inspection of the bag and the solutions before mixing is necessary. Particular attention should be paid to even the slightest damage to the closure, the welded seam and the corners of the bag in view of a possible contamination.
2. Mixing of the two compartments
   The two-compartment-bag - the bicarbonate and the electrolytes including glucose compartments - are mixed immediately before use to obtain a ready-for-use solution.

A)

Unfold the small compartment.

B)

Roll up the solution bag starting from the corner opposite the small compartment....

C)

... until the peel seam between both compartments has opened along its entire length and the solutions from both compartments are mixed.

After mixing both compartments, it must be checked, that the peel seam is completely open, that the mixed solution is clear and colourless and that the bag is not leaking.

3. Application of the ready-to-use solution
   The ready-to-use solution must be used immediately, but within a maximum of 48 hours after mixing.
   Any admixture to the ready-to-use solution must only be done after the ready-to-use solution has been thoroughly mixed. After such an admixture, the ready-to-use solution should again be thoroughly mixed prior to use.
   Admixtures of sodium chloride solution (concentration between 3% and 30% sodium chloride; up to 250 mmol sodium chloride per 5 litre multiBic solution) and water for injection (up to 1250 ml per 5 litre multiBic solution) are compatible with this medicinal product.
   If not otherwise prescribed, the ready-to-use solution should be warmed immediately before use to 36.5°C – 38.0°C. The exact temperature must be selected depending on clinical requirements and the technical equipment used.
   No special requirements for disposal.

8. Contraindication

Solution related contraindications
- Hypersensitivity to the active substances or to any of the excipients listed in section 2
- Hypokalaemia
- Metabolic alkalosis

Contraindications for use of the technical procedure itself
- Inadequate blood flow from vascular access.
- If there is a high risk of haemorrhage on account of systemic anticoagulation.

9. Warnings and Precautions

Use only after mixing of the two solutions.
multiBic® 2 mmol/L potassium should be warmed prior to use with appropriate equipment to approximately body temperature and must not be used under any circumstances below room temperature.
The warming of the ready-to-use solution to approximately body temperature must be carefully controlled verifying that the ready-to-use solution is clear and without particles.
During application of the ready-to-use solution, white calcium carbonate precipitation has been observed in the tubing lines in rare cases, particularly close to the pump unit and the heating unit warming the ready-to-use solution.
Precipitations particularly can occur if the temperature of the ready-to-use solution at the inlet of the pump unit is already higher than 30°C.
Therefore, the ready-to-use solution in the tubing lines must be closely visually inspected every 30 min during continuous renal replacement therapy in order to ensure, that the solution in the tubing system is clear and free from precipitate. Precipitations may occur also with substantial delay after start of treatment.
If precipitate is observed, the ready-to-use solution and the tubing lines used for continuous renal replacement therapy must be replaced immediately and the patient carefully monitored.
The serum potassium concentration must be checked regularly before and during continuous renal replacement therapy. The potassium status of the patient and its trend during the treatment must be considered.
In case of hypokalaemia supplementation of potassium and / or changing to a solution for haemodialysis/haemofiltration with higher potassium concentration may be required.
In case of hyperkalaemia an increase in the applied dose and / or change to a solution for haemodialysis/haemofiltration with a lower potassium concentration may be indicated as well as usual measures of intensive care medicine.
The serum sodium concentration must be checked regularly before and during use of this solution for haemodialysis/haemofiltration to control risks related to hypo/ hypernatremia. The solution for haemodialysis/haemofiltration may be diluted with an adequate amount of water for injections or concentrated sodium chloride solution may be added if required. The speed of desired normalisation must then be carefully planned to avoid adverse reactions due to rapid changes in serum sodium concentration.
In addition, the following parameters must be monitored before and during continuous renal replacement therapy: Serum calcium, serum magnesium, serum phosphate, serum glucose, acid-base status, levels of urea and creatinine, body weight and fluid balance (for the early recognition of hyper- and dehydration).
Clinically important substances may be removed with the haemodialysis, haemofiltration and haemodiafiltration treatment and are not supplemented with this medicinal product. This removal of important nutrients must be compensated by adequate nutrition, nutritional supplements, or an adapted parenteral nutrition.
Paediatric population
There is no clinical experience on the use of this product in children. This medicinal product is not recommended for use in children until further data become available (see sections 7 and 4.1).

10. Interactions With Other Medicaments

No interaction studies have been performed.
The correct dose of multiBic® 2 mmol/L potassium and strict monitoring of clinical chemistry parameters and vital signs will avoid risks related to interactions with other medicinal products.
The following interactions are conceivable:
- Toxic effects of digitalis may be masked by hyperkalaemia, hypermagnesaemia and hypocalcaemia. The correction of these electrolytes by continuous renal replacement therapy may precipitate signs and symptoms of digitalis toxicity, e.g. cardiac arrhythmia.
- Electrolyte substitutions, parenteral nutrition and other infusions usually given in intensive care medicine interact with the serum composition and the fluid status of the patient. This must be considered during application of continuous renal replacement therapy.
- Continuous renal replacement therapy may reduce the blood concentration of drugs, especially of drugs with a low protein binding capacity, with a small distribution volume, with a molecular weight below the cut-off of the haemofilter and of medicinal products adsorbed to the haemofilter. An appropriate revision of the dose of such medicinal products may be required.

11. Pregnancy and Lactation

There are no or limited amount of data from the use of multiBic® 2 mmol/L potassium in pregnant women. Animal studies are insufficient with respect to reproductive toxicity.
multiBic® 2 mmol/L potassium should not be used during pregnancy unless the clinical condition of the woman requires continuous renal replacement therapy.
There is insufficient information on the excretion of multiBic® 2 mmol/L potassium active substances/metabolites in human milk.
Breastfeeding is not recommended during treatment with multiBic® 2 mmol/L potassium.

12. Undesirable Effects

Adverse reactions may result from the treatment mode itself or may be induced by this medicinal product:
Gastrointestinal disorders - nausea, vomiting
Vascular disorders - hypertension, hypotension
Musculoskeletal and connective tissue disorders - muscle cramps
The following adverse reaction can be anticipated for the treatment mode:
Metabolism and nutrition disorders - hyper- or hypothydration, electrolyte disturbances (e.g., hypokalaemia), hypophosphataemia, hyperglycaemia, and metabolic alkalosis.
The exact frequency of such events is not known (cannot be estimated from the available data).

13. Overdose and treatment

After use of recommended doses no reports of emergency situations have arisen; moreover, the administration of this medicinal product can be discontinued at any time. If fluid balance is not accurately calculated and monitored, hyperhydration or dehydration may occur, with the resultant associated circulatory reactions. These may be manifest through changes in blood pressure, central venous pressure, heart rate, and pulmonary arterial pressure. In cases of hyperhydration congestive cardiac failure and/or pulmonary congestion may be induced.
In cases of hyperhydration, net fluid removal should be increased on the device used for continuous renal replacement therapy. In cases of marked dehydration, net fluid removal by the device used for continuous renal replacement therapy should be decreased or discontinued; alternatively, fluid resuscitation can be applied to restore the hydration status.
If too large volume is applied, this may result in disturbances of electrolyte concentrations and the acid-base-balance, e. g. an overdose of bicarbonate may occur if an inappropriate large volume of the solution for haemodialysis/haemofiltration is infused / administered. This could possibly lead to metabolic alkalosis, decrease of ionized calcium, or tetany.

14. Storage Condition

Store below 30°C. Do not store below 4°C. Keep out of reach and sight of children.
Shelf life: 24 months
Chemical and physical in-use stability of the ready-to-use solution has been demonstrated for 48 hours at 30 °C. It is not recommended to store the ready-to-use solution longer than 48 hours including duration of treatment or at a temperature higher than 30 °C prior to the inlet of the pump unit.
From a microbiological point of view, once connected to the haemodialysis, haemofiltration or haemodiafiltration circuit, and as hydrogen carbonate is present, the product shall be used immediately.

15. Dosage Forms and packaging available

multiBic® 2 mmol/L potassium is delivered in a double chamber bag (two-compartment). Mixing of both solutions by opening the seam between the two chambers result in the ready-to –use solution for haemofiltration.
Each bag contains 5000 mL solution in total.
Pack size: 2 bags of 5000mL

16. Name and Address of Manufacturer/Marketing Authorization Holder/ Product Registration Holder

Marketing Authorization Holder
Fresenius Medical Care Deutschland GmbH
Else-Kröner-Straße 1
61352 Bad Homburg v.d.H
Germany
Manufacturer
Fresenius Medical Care Deutschland GmbH
Frankfurter Straße 6-8,
66606 St. Wendel, Germany
Product Registration Holder
Fresenius Medical Care Philippines, Inc.
18/1 Aeon Center, corner Alabang-Zapote Road and North Bridgeway, Filinvest Corporate City, Alabang, Muntinlupa City 1781, Philippines.

17. Caution

Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

18. ADR Reporting

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.

19. Registration number

DR-XY00000000

20. Date of first Authorization/Renewal of Authorization

21. Date of Revision of Package Insert

The insert was last revised in September 2017

FRESENIUS MEDICAL CARE
THE RENAL COMPANY

multiBic® 2 mmol/L potassium solution for haemodialysis/haemofiltration

AUSTRALIA/SINGAPORE
Package Leaflet

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 nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What multiBic® 2 mmol/l potassium is and what it is used for

multiBic® 2 mmol/l potassium is a continuous renal replacement therapy solution for removal of waste products from the body in people with kidney disease. It is used in patients with kidney injury and also for the treatment of poisoning. The type of solution you are given depends on the amount of potassium (a salt) in your blood. Your doctor will check your potassium levels regularly.

2. What you need to know before you use multiBic® 2 mmol/l potassium

Do not use multiBic® 2 mmol/l potassium if
- you are allergic to any of the active substances or any of the other ingredients of this medicine (listed in section 6)
- you have hypokalaemia (your potassium level is very low)
- you have metabolic alkalosis (a condition where there is too much bicarbonate in the blood)
- you cannot achieve a sufficient blood flow through the haemofilter (filter used in the blood filtration)
- you have a high risk of bleeding related to medications required to prevent clotting in the haemofilter

Warnings and precautions

Talk to your doctor before using multiBic® 2 mmol/l potassium.
- Must be used only after mixing the two solutions in the double chamber (two-compartment) bag.
- Must not be used under any circumstances below room temperature.
- The tubing lines used to apply the ready-to-use solution should be inspected every 30 minutes. If precipitate (solid matter) is observed within these tubing lines, bag and tubing lines must be replaced immediately and the patient carefully monitored.
- Your doctor will check your hydration status (the amount of water in your body), the levels of potassium, sodium, other salts, certain waste products, and your blood sugar levels. Your doctor also might advise you about your diet.

Children

Use of multiBic® 2 mmol/l potassium has not been established in children.

Other medicines

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

Following interactions are conceivable:
- toxic effects of digitalis (medicine for treatment of heart disease)
- electrolyte substitutions, parenteral nutrition (intravenous feeding) and other infusions treatment. Their effect on blood serum concentration and fluid status must be considered when using this therapy
- This therapy may reduce the blood concentration of medicinal products. Dose adjustment may be required.

Pregnancy and breast-feeding

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 starting treatment with this medicine.

There are no or limited amount of data on the use of multiBic® 2 mmol/l potassium during pregnancy and breast-feeding.

This medicine should only be used during pregnancy if your doctor considers treatment necessary.

Breast-feeding is not recommended during treatment with multiBic® 2 mmol/l potassium.

3 How to use multiBic® 2 mmol/l potassium

multiBic® 2 mmol/l potassium will be given in a hospital or clinic. Your doctor will know how to use this medicine.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The side effects of multiBic® 2 mmol/l potassium include:
- nausea (feeling sick)
- vomiting (being sick)
- muscle cramps
- changes in blood pressure

Some side effects might be caused by too much or too little fluid. These are:
- shortness of breath
- swelling of the ankles and legs
- dehydration (e.g. dizziness, muscle cramps, feeling thirsty)
- blood disorders (e.g. abnormal salt concentrations in your blood)

The exact frequency of such events is not known (cannot be estimated from the available data).

Reporting of side effects

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

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

5. How to store multiBic® 2 mmol/l potassium

Your doctor knows how to store multiBic® 2 mmol/L potassium.

Store below 30°C. Do not store below 4°C.

6. Content of the pack and other information

What multiBic® 2 mmol/l potassium contains
- The active substances are potassium chloride, sodium chloride, sodium hydrogen carbonate, calcium chloride dihydrate, magnesium chloride hexahydrate, glucose monohydrate.
- The other ingredients are water for injections, hydrochloric acid 25 %, carbon dioxide and sodium dihydrogen phosphate dihydrate.

What multiBic® 2 mmol/l potassium looks like and contents of the pack

multiBic® 2 mmol/l potassium is delivered in a double chamber bag (two-compartments containing different solutions). Mixing of the solutions in both compartments results in the ready-to-use solution.

Each bag contains 5000 ml solution in total. The ready-to-use solution is clear and colourless.

Each bag is equipped with a HF-connector, a Luer-lock-connector and an injection port, and is covered by a protective foil.

Pack size:
2 bags of 5000 ml

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder

Fresenius Medical Care Deutschland GmbH, Else-Kröner-Straße 1, 61352 Bad Homburg v.d.H., Germany

Manufacturer

Fresenius Medical Care Deutschland GmbH, Frankfurter Straße 6-8, 66606 St. Wendel, Germany

Imported and Distributed by:

Fresenius Medical Care Singapore Pte Ltd. Singapore

Fresenius Medical Care Australia Pty. Ltd.

305 Woodpark Road, Smithfield NSW 2164 Sydney, Australia

This leaflet was last revised in July 2017.

Information for healthcare professionals only see end of this package leaflet.

The following information is intended for healthcare professionals only:

1000 ml of the ready-to-use solution contain:

Potassium chloride	0,1491 g
Sodium chloride	6.136 g
Sodium hydrogen carbonate	2.940 g
Calcium chloride dihydrate	0.2205 g
Magnesium chloride hexahydrate	0.1017 g
Glucose monohydrate	1.100 g
(Glucose)	(1.000 g)
K^+	2.0 mmol/l
Na^+	140 mmol/l
Ca^{2+}	1.5 mmol/l
Mg^{2+}	0.50 mmol/l
Cl^-	111 mmol/l
HCO_3^-	35 mmol/l
Glucose	5.55 mmol/l

pH ≈ 7.4

Theoretical osmolarity (Theor. osmolar.) 296 mOsm/l

Do not use unless the ready-to-use solution is clear and colourless and the bag and connectors are undamaged.

For single use only. Any unused solution must be discarded.

Must be used by means of metering pumps.

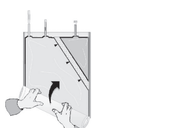
Instructions for use

1. Removal of the protective foil and careful inspection of the bag containing the haemofiltration solution
   The protective foil should only be removed immediately before using the solution.
   Plastic containers may occasionally be damaged during transport from the manufacturer to the dialysis clinic or hospital clinic or within the clinic itself. This can lead to contamination and the growth of bacteria or a fungus in the solution for haemofiltration. Therefore careful inspection of the bag and of the solution before use is necessary.
   Particular attention should be paid to even the slightest damage to the closure of the bag, the welded seam and the corners of the bag. The solution should only be used if clear and colourless and if the container (the bag) and connectors are undamaged and are intact.
   In case of doubt the doctor should decide whether the haemofiltration solution should be used or not.
2. Mixing of the solutions in the double chamber bag.
   The two solutions should be mixed immediately before use to produce a solution ready-to-use. The solution is clear and colourless.

A)

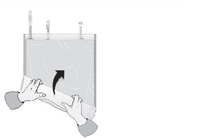
Unfold the small compartment.

B)



Roll up the solution bag starting from the corner opposite the small compartment ....

C)



... until the peel seam between both compartments has opened along its entire length and the solutions from both compartments are mixed.

After mixing both compartments, it must be checked, that the peel seam is completely open, that the solution is clear and colourless and that the container is not leaking.

3. Ready-to-use solution
   If prescribed, medicinal products (drugs) may be added to the readyto- use haemofiltration solution. This should only be carried out after the seam between the two chambers has been fully opened and the two solutions have been thoroughly mixed. The addition of any drugs to the haemofiltration solution would only be carried out on the doctor's advice and care must be taken not to introduce any contamination into the bag. After a drug has been added to the haemofiltration solution, the solution should be thoroughly mixed again before administration of the solution to the patient. The bags should be labeled with details of the name and amount of drug, together with the time and date.
   The ready-to-use solution shall be used immediately, not stored above +25°C and must be used within a maximum of 48 hours after mixing. Chemical and physical in-use stability of the ready-to-use solution has been demonstrated for 48 hours at 25°C. Other in-use storage times and conditions prior to use (longer than 48 hours including the duration of the treatment, higher than 25°C prior to the inlet of the pump unit) are the responsibility of the user.From a microbiological point of view, once connected to the haemofiltration circuit, and as hydrogen carbonate is present, the product shall be used immediately. Other in-use storage times and conditions are the responsibility of the user.
   The haemofiltration solution should be warmed prior to infusion with appropriate equipment to approximately body temperature and must not be infused under any circumstances below room temperature.
   The warming of this solution to approximately body temperature must be carefully controlled verifying that the solution is clear and without particles. If not otherwise prescribed, the ready-to-use solution for haemofiltration should be warmed immediately before infusion into the patient to 36.5°C - 38°C. The exact temperature must be selected on the doctor's advice depending on the clinical need. Only devices approved for warming haemofiltration solutions must be used. The use of a dedicated device for haemofiltration treatments which will also warm the solutions for haemofiltration prior to infusion is recommended. Microwave ovens must not be used to warm multiBic® 2 mmol/L potassium due to the possibility of local overheating.
   During application of multiBic in CRRT, white calcium carbonate precipitation has been observed in the tubing lines in rare cases, particularly close to the pump unit and the heating unit warming multiBic. Precipitations particularly can occur if the temperature of the multiBic solution at the inlet of the pump unit is already higher than 25°C. Therefore, the multiBic solution in the tubing lines should be closely visually inspected every 30 min during CRRT in order to ensure, that the solution in the tubing system is clear and free from precipitate. Precipitations may occur also with substantial delay after start of treatment. If precipitate is observed, multiBic solution and CRRT tubing lines must be replaced immediately and the patient carefully monitored.
   The haemofiltration solution is for single use only; any unused solution and any damaged containers should be discarded.

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