SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active ingredients :
Each 100 ml solution contains:
Dextrose monohydrate: 5 g
Sodium chloride: 0.60 g
Sodium lactate: 0.30 g
Potassium chloride: 0.03 g
Calcium chloride dihydrate: 0.02 g

Electrolyte concentrations in the solution, mEq/l (mmol/l):
- Sodium: 129 (129)
- Chloride: 109 (109)
- Potassium: 4 (4)
- Lactate: 27 (27)
- Calcium: 3 (1.5)

pH of the solution is in the 4.0-6.5 range.

Excipients:
See section 6.1 for excipients.

3. PHARMACEUTICAL FORM
Sterile and apyrogen solution for intravenous infusion

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
- For extracellular fluid replacement where electrolytes is isotonic concentrations are inadequate or with the purpose of restoration of the electrolyte balance.

- With the purpose of short-term volume replacement in cases to hypovolemia or hypotension (alone or together with a colloid solution)

- To regulate or maintain the balance in metabolic acidosis and/or for the treatment of metabolic acidosis with mild-medium severity (excluding lactic acidosis).

4.2. Posology and method of administration
Posology/ Frequency and period of administration

The dosage to be administered must be decided individually for each patient by the doctor based on the age, body weight, and clinical conditions and particularly on the hydration status of the patient.

POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION will be required in 3-5 folds of the amount lost in order to restore the blood volume.

Adults: 500-3000 ml/day

Infants and children:
- 0-10 kg: 100 ml/kg/day
- 10-20 kg: 1000 ml+50 ml/day for each kilogram weight over 10 kg
- > 20 kg: 1500 ml +20 ml/day for each kilogram weight over 20 kg

Infusion rate and the total administered volume can be increased in operations and wherever required.

Route of administration:
Administration is made through sterile apyrogen sets.
Please see section 6.6 for details of administration.

Administration rate:
The infusion rate in adults is 40 ml/kg per day.
The mean administration rate of 5 ml/kg/day is recommended for pediatric cases (6-8 ml/kg/hour for infants, 4-6 ml/kg/hour for pre-school children and 2-4 ml/kg/hour for school children).

Special populations:
Renal/ hepatic impairment:
Since there are no studies performed specifically on this population, there are no special dosages recommended for this patient group.

Since lactate metabolism can be impaired in patients with liver failure, the alkalizing effect of POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION can fail.

Paediatric population:
Like in the adults, the dosage to be administered and the infusion rate will be adjusted according to the weight and clinical and biological status of the patient and also according to the treatment to be administered concomitantly.

In children with burns, 3.4 ml/kg/burn ratio must be administered within the first 24 hours and 6.3 ml/kg/burn ratio must be administered within the second day.

The mean dosage in children with serious head trauma is 2850 ml/m^2.

Geriatric population:
Like in the adults, the dosage to be administered and the infusion rate will be adjusted by the doctor according to the weight and clinical and biological status of the patient and also according to the treatment to be administered concomitantly.

4.3. Contraindications

The solution is contraindicated in patients with the following conditions:
- Extracellular hyperhydration or hypervolemia
- Severe renal failure (accompanied by oliguria/anuria)
- Decompensated cardiac failure
- Hyperkalemia
- Hypernatremia
- Hypercalcemia
- Hyperchloremia
- Metabolic alkalosis
- Severe metabolic acidosis
- Lactic acidosis
- Severe hepatocellular failure or conditions that lactate metabolism is impaired
- Cirrhosis with a course of general edema and ascites

Furthermore, the solution is contra-indicated in decompensated diabetes, other glucose tolerance disorders (including the metabolic stress), hyperosmolar coma, hyperglycemia and hyperlactatemia.

In infants younger than 28 days, use of POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION together with ceftriaxone is contra-indicated - even if used through separate infusion lines (fatal accumulation of the calcium salt of ceftriaxone in the blood circulation of the neonate).

In patients older than 28 days (including adults), ceftriaxone must not be administered simultaneously through the same infusion line (e.g., through a Y-line) with solutions containing calcium including POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION. If the same application set will be used for consecutive applications, the set must be irrigated thoroughly with compatible solutions.

4.4 Special warnings and precautions for use

Administration of the intravenous solutions can lead to dilution of the serum electrolyte concentrations, over-hydration, and overloading of fluid and/or solute to cause congestive conditions and/or pulmonary edema. The risk of dilution is inversely proportional with the electrolyte concentration. The risk of developing congestive conditions that lead to peripheral or pulmonary edema, however, is directly proportional with the electrolyte concentrations in the solution.

POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION is a solution with approximate osmolarity of 523 mOsml/l.

Solutions of high volumes must be administered with special care in patients with cardiac or pulmonary insufficiency.

Clinical status and laboratory parameters (electrolyte levels in blood and urine and acid-base balance) of the patient must be followed closely during the use of this solution. Close monitoring of potassium is particularly necessary in patients under the risk of hyperkalemia.

Solutions containing sodium chloride must be used carefully in hypertension, cardiac insufficiency, peripheral or pulmonary edema, or where the renal functions are impaired, in preeclampsia, aldosteronism or other conditions and treatments having courses involving sodium accumulation (See also Section 4.5).

Solutions containing potassium must be used carefully in patients with cardiac patients or in cases of adrenocortical insufficiency, acute dehydration or excessive tissue damage that create predisposition to hyperkalemia.

Although the potassium amount in the composition of POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION is similar to that of contained in the plasma, its level is not adequate to create a beneficial effect in severe potassium insufficiency conditions and must not be used with this purpose.

Calcium chloride is irritating; therefore, care must be given to prevent leakage of the solution outside the vein. Solutions containing calcium salts must be used carefully in patients with impaired renal functions or with high levels of vitamin D like in patients with sarcoidosis. In addition, its use must be avoided in patients with renal calcium stones in their history. If blood transfusion will be made simultaneously, administration through the same infusion system is not recommended because of the risk of coagulation by the calcium content.

Proper nutritional support must be provided for the patient during long-term parenteral treatments.

POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION can lead to metabolic alkalosis conditions because of the lactate ions it contains.

Since the lactate metabolism can be impaired in patients with liver insufficiency, POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION may not show its alkalizing effect.

Lactate-containing solutions must be used carefully in infants younger than 6 months.

Use of lactate-containing solutions can lead to hyperglycemia. The infusion rate must be adjusted or insulin must be administered in case of hyperglycemia.

The insulin dose administered to the diabetic patients must be re-adjusted based on the amount of glucose administered.

With the purpose of minimizing the risk compatibility with any drug that might be added to the solution, turbidity or sedimentation must be checked in the final solution to be infused immediately after mixing and with certain intervals during the administration.

In case the administration will be made through a controlled infusion pump, it must be checked if the operation of the pump has been stopped before the complete emptying of the bag; otherwise, air embolism can result.

In order to avoid the air embolism related to the residual air remained in the primary bag, do not connect flexible plastic bags serially.

Squeezing the bag to increase the flow rate during administration can cause air embolism if the air within the bag has not been discharged completely.

Use of an intravenous application set with an airway when this airway is open can result in air embolism. Intravenous infusion application sets with airways must be used in for the infusion of solutions within plastic bags when the airway is open.

Lactate is a substrate of gluconeogenesis. This must be taken into consideration when POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION is used in patients with type 2 diabetes.

<u>Use in paediatric patients</u>

• The effectiveness and safe use of POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION in children have not been investigated in well-controlled

studies; however, there are data in the medical literature showing the use of solutions containing electrolytes in the pediatric population.

• Lactate-containing solutions must be administered with special care to neonates and infants younger than 6 months of age.

Use in geriatric patients
It must be kept in mind when determining the type and administration rate and volume of infusion solutions in geriatric patients that cardiac, renal, liver and other patients and chronic drug use is more frequent in this age group.

The solution is used intravenously through sterile sets. Replacing the sets used in intravenous applications every 24 hours is recommended.

Use only if the solution is clear and if the packaging and caps are intact.

4.5. Interaction with other medicinal products and other forms of interaction
Interactions with sodium contained in the solution:

- Corticoids/steroid and carbenoxolone related to retention of sodium and water (together with edema and hypertension).

Interactions related to the potassium contained in the solution:

- Potassium retaining diuretics (amiloride, spironolactone or triamterene singly or in combination).
- Angiotensin converting enzyme inhibitors and possible anjiyotensin II receptor antagonists.
- Tacrolimus and cyclosporine (these drugs increase the potassium concentration in the plasma and can potentially cause fatal hyperkalemia in renal failure conditions, in which the hyperkalemic effects will increase).

Interactions related to the calcium contained in the solution:

- Digitalis group glycosides with effects that increase in the presence of calcium and can cause serious or fatal cardiac arrhythmias.
- Tiazide group diuretics or vitamin D that can cause hypercalcemia when administered together with calcium.
- Biphosphonates, fluoride, some fluorokinolones and tetracyclines that absorptions are reduced when administered together with calcium
- Ceftriaxone - because of the risk of ceftriaxone-calcium precipitation that can be fatal when administered together with calcium (See: Section 4.3. Contra-indications).

Interactions with the lactate contained in the solution (lactate is metabolized to bicarbonate):

- Since bicarbonates resulting from lactate metabolism render urine alkaline, renal excretion of acidic drugs including salicylates, barbiturates and lithium will increase.
- However, half lifes of alkaline drugs including sympathomimetic drugs (e.g. ephedrine, pseudoephedrine) and stimulant drugs (e.g. dexamphetamine sulfate, fenfluramine hydrochloride) will increase because of slower elimination.

4.6 Pregnancy and lactation

General recommendations

Pregnancy category: C.

Women of childbearing potential /Contraception

Adequate data related to the use of dextrose solutions containing sodium chloride in pregnant women are not available. Studies carried out on animals are inadequate as regards the effects on pregnancy and/or embryonic /fetal development and/or natal/ postnatal development (see: Section 5.3). Potential risks on humans are not known.

Pregnancy

Studies on animal reproduction with POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR IV INFUSION has not been carried out. Whether or not POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION causes fetal damage if used in pregnant women, or if it causes impairment on ability of fertility are not known. POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION must be used with care in pregnant women.

POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION can be used during pregnancy and lactation with the provision that electrolyte and fluid balance is kept under control.

It must be kept in mind that calcium can pass the placenta.

Lactation

It is not whether or not this drug is excreted to the breast milk. Since it is known that many drugs are excreted in the breast milk, POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION must be used carefully in breastfeeding mothers.

It must be kept in mind that calcium is distributed to breast milk.

In case any drug will be added to the solution, the properties of this drug and its effects on pregnancy or lactation must be evaluated separately.

Fertility

In has no known effects.

4.7 Effects on ability to drive and use machines
Driving is practically impossible during the use of solutions administered through infusion. It has no known effects on driving or use of machines following the intake.

4.8 Undesirable effects
Adverse effects related to the application technique include febrile reactions, infection at the injection site, venous thrombosis or phlebitis starting from the injection site and spreading, phlebitis, extravasation and hypervolemia.

The classification of the frequency and severity of the adverse drug reactions seen with the use of POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR IV INFUSION are as follows: very common (≥1/10); common (≥1/100 to <1/10); not common (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), and unknown (available data do not allow deciding)

Immune system disorders
Very common: Allergic reactions or localized or widespread urticaria anaphylactic/anaphylactoid reactions including skin rashes, erythema or itching/pruritus; swelling of the skin, edema around eyes, face and/or larynx (Quincke's edema)

Metabolism and nutrition disorders
Common: Electrolyte disturbances

Psychiatric disorders
Common: Anxiety
Vary rare: Panic attack

Nervous system disorders
Uncommon: Contractions stimulated by alkalosis related to lactate

Cardiac disorders
Very common: Hyper-hydration and cardiac insufficiency (in patients with cardiac diseases or pulmonary edema).
Common: Tachycardia, bradycardia

Respiratory, thoracic and mediastinal disorders
Very common: Nasal congestion, cough, sneezing, bronchospasm and/or difficulties in breathing
Common: Feeling of compression on the chest, chest pain (together with tachycardia or bradycardia)

Skin and subcutaneous tissue disorders
Very common: Itching (Approximately 10% of the patients that have used POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION has reported pruritus).

It must be kept in mind that the drugs administered after dilution also can cause adverse effects. In such cases, the product information of the additional drug administered must be referred to.

Infusion must be stopped in case of adverse effects, the patient must be evaluated, proper therapeutical measures must be taken and the residual drug within the bag must be kept for examination if needed.

4.9. Overdose and treatment
Administration of overdose or very rapid administration can cause water and sodium overloading resulting in the risk of edema in cases where the renal sodium excretion is impaired. Renal dialysis therapy can be required in such cases.

Administration of potassium in excessive amounts can cause hyperkalemia in patients with renal failure. Symptoms of hyperkalemia include paresthesia in extremities, muscular weakness, paralysis, cardiac arrhythmias, cardiac blockage, cardiac arrest and mental confusion.

Administration of excessive calcium can cause hypercalcemia. Symptoms of hypercalcemia include anorexia, nausea, vomiting, constipation, abdominal pain, muscular weakness, mental disorders, polydipsia, polyuria, nephrocalcinosis, and formation of renal stones and in more severe cases, cardiac arrhythmias and coma. Too fast infusion of calcium salts can cause chalk-like taste in the mouth, sudden flushing in the body and particularly in the face and peripheral dilation, as well as many other symptoms of the hypercalcemia. Mild asymptomatic hypercalcemia returns to normal by stopping the administration of calcium and drugs contributing to hypercalcemia including vitamin D. In case hypercalcemia is serious, treatments including loop diuretics, hemodialysis, calcitonin, biphosphonate and trisodium edetate must be started urgently.

Administration of excessive sodium lactate can cause hypokalemia and metabolic alkalosis particularly in patients with renal insufficiency. Symptoms include mood changes, fatigue, stopping of breathing, muscular weakness and irregularity of the heartbeats. Muscular hypertonicity, fasciculation and tetanus can be seen especially in hypocalcemic patients. Treatment of the metabolic alkalosis related to overdose of bicarbonate mainly includes the proper regulation of the fluid and electrolyte balance.

Replacement of calcium, chloride and potassium deficiencies is particularly important.

Long-term administration or administration in excessive amounts of solutions containing dextrose will cause hyperglycemia and consequent hyperosmolarity, dehydration and osmotic diuresis.

If overdose is related to the drugs added to the solution, the signs and symptoms related to overdose will depend on the added drug.
If the dosage is inadvertently exceeded during the treatment, administration must be stopped and the patient must be followed for the signs and symptoms of the administered drug. Symptomatic and supporting treatments must be administered if required.

5. PHARMACOLOGICAL PARTICULARS

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Electrolyte solutions containing carbohydrates
ATC code: B05BB02

Pharmacodynamic properties of POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION consists of the properties of its components (glucose, sodium, potassium, calcium, chloride and lactate).

Glucose is the main energy source in the cellular metabolism. Dextrose solutions provide calories and water required for hydration for the body. Such solutions can stimulate diuresis depending on the clinical conditions of the patients. Glucose is fully metabolized and decreases the protein and nitrogen losses in the body, and increases glycogen storage. It decreases or prevents ketosis when administered in adequate dosages.

Ions like sodium pass through the cellular membrane using various transport mechanisms include sodium pump (Na-K-ATPase). Sodium plays an important role in nerve transmission, cardiac electrophysiology and renal metabolism.
Sodium is the main cation of the extracellular fluid. The normal sodium level in the serum is in the 135- 145 mEq/l range. Sodium levels as the basic regulator of body fluids are kept within a rather fixed level through several mechanisms. For example, when serum sodium levels increase, secretion of the antidiuretic hormone decreases, and sodium is excreted from the kidneys; while secretion of the antidiuretic hormone increases upon reduction of sodium levels in an attempt to maintain serum sodium levels.
Sodium shows its effect primarily on the water distribution in the body, fluid balance and control of the osmotic pressure of the body fluids. Sodium is also related to the regulation of the acid-base balance in body fluids together with chloride and bicarbonate.

The normal serum levels of chloride, which is the main anion of the extracellular fluid, is in the 100-106 mEq/l range, closely follows the sodium metabolism and changes in the acid-base balance of the body is reflected in the changes in chloride concentration. Chloride is found in the bony tissue in small amounts, while it is found in high amount in some components of the connective tissues, e.g. in the collagen tissue. Intracellular chloride is found in high concentrations in the erythrocytes and gastric mucosa. Balance of anions and cations in the body is regulated through the kidneys. Re-uptake of chloride generally follows the re-uptake of sodium.

Potassium is the main cation of the intracellular fluid, and it is required for the maintenance of the acid-base balance, isotonicity, and the electrodynamic characteristics of the cell. Potassium is important re-activator for many enzymatic reactions; it is vitally important for many physiological processes including the transmission of the nerve impulses, contractility of the cardiac and skeletal muscles, gastric secretions, renal functions, tissue synthesis and carbohydrate metabolism.

The normal potassium level in the serum is in 3-4.5 mEq/l range. Kidneys rapidly eliminate potassium from body when the level of this ion increases.
Potassium deficiency presents itself through the impairment of neuromuscular function, dilatation of intestines and ileus.

Lactate included in the composition of the solution will be transformed into bicarbonate mainly in the liver and has an alkalizing effect in the plasma.

Since POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION contains chloride, lactate and other important cations in the extracellular fluids, it is among the most appropriate solutions for the parenteral fluid treatment. In large fluid losses of the body, the fluid-electrolyte balance of the patient can be ensured with this solution without changing the making changes in the composition of the extracellular fluids.

If acid-base balance in the organism shifts to the acidic side, the basis of the treatment is to increase the bicarbonate levels in the extracellular fluid. Since direct administration of sodium bicarbonate can be dangerous, lactated solutions are used with this purpose. Lactate ions are metabolized in the liver and replace the bicarbonate ions; and thus increase the plasma bicarbonate levels.POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION eliminates the acidosis in metabolic acidosis and also meets the extracellular fluid loss, which is always present in such cases.

The central venous pressure changes seen in the healthy volunteers that POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION was administered to has been found related to the secretion of atrial natriuretic peptide. This solution increases the serum

osmolarity in healthy volunteers, increases the blood pH and initial urination is seen in a shorter period of time as compared to sodium chloride solutions with physiologic concentrations.

Statistically significant changes were not found in glucagon, noradrenalin, adrenalin, blood glucose or insulin levels in patients undergoing aortic surgery with POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION.

The pharmacodynamic of the solution will change according to the properties of the drug added to POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION.

5.2 Pharmacokinetic properties

Pharmacokinetic properties of POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION consist of the pharmacokinetic properties of its components (glucose, sodium, potassium, calcium, chloride and lactate).

Absorption:
The active ingredients in the drugs administered through the intravenous route reach the maximum plasma concentrations immediately after the administration.

Distribution:

Glucose is the basic monosaccharide that is distributed in all the cells and meets the energy requirement of the body. Insulin is required for the entry of glucose to cells other than erythrocytes.

The half-life following radioactive-labeled sodium (^{24}Na) injection is 11 to 13 days for 99% of the injected sodium, and one year for the remaining 1%. Distribution differs according to tissues: it is fast in the muscle, liver, kidneys, cartilage and skin, slow in erythrocytes and neurons, and very slow in bones.

Potassium in the extracellular fluid enters the cell with active transport until it reaches 40 times of the extracellular concentration. Glucose, insulin and oxygen make the entry of potassium into cell easier. The plasma potassium concentration in healthy adults is in 3.5-5 mEq/l range. The plasma level in neonates can reach 7.7 mEq/L. Together with this, since the plasma levels of potassium do not fully reflect the intracellular potassium levels, cellular hypokalemia can be present despite the normal plasma levels. Changes of pH in the extracellular fluid also cause changes in the plasma potassium concentration. A change in the plasma pH of 0.1 units can cause a 0.6 mEq/l reverse change in the plasma potassium concentration.

Chloride is normally found in low amounts in the bony tissue and in large amounts in some components of the connective tissue, for example, in the connective tissue. Together with this, it is also found in high concentrations in the erythrocytes and gastric mucosa. The levels of chloride, which is the main anion in the extracellular fluid, in the body are closely related to the changes in the sodium concentration. Abnormalities in the sodium metabolism generally result in changes also in the chloride concentration.

Calcium is an important cation for the maintenance of life both in intracellular and extracellular level. It either stays in the plasma or distributed to tissues based on the requirement. Calcium is also excreted to the placenta and breast milk.

Pharmacokinetics of D-lactate and L-lactate resemble each other. POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION will not increase the lactate amounts in circulation in normal adults who are stable as regards hemodynamics. Lactate is transformed into bicarbonate through oxidation in serum. Lactate distributed to liver is transformed into bicarbonate through gluconeogenesis.

Biotransformation:
Glucose is easily and fully metabolized in the body through pyruvic acid or lactic acid route and provides energy while largely turning into carbon dioxide and water. Glucose can be administered without causing glucosuria with dosages up to 0.5 g/kg. Approximately 95% of the administered glucose will remain in the body is administered with a rate of 0.8g/kg, which is the highest infusion rate.

Sodium, potassium, calcium and chloride do not undergo any biotransformation. They are either distributed in the body fluids or tissues or are eliminated.

Lactate however, is metabolized to bicarbonate both with oxidation and particularly with gluconeogenesis in the liver within about 1-2 hours.

Elimination:
Glucose, which is transformed into carbon dioxide and water, is normally excreted as carbon dioxide with expiration and as water through the kidneys. When the glucose level exceeds 160-180mg %, which is the renal threshold for glucose, it can also be excreted directly through the kidneys (glukosuria).

Sodium is mainly excreted through the renal route; the great majority is re-absorbed through the renal route. Small amounts of sodium are excreted with feces and sweat. Excretion through the skin is insignificant unless sweating is excessive.

Chloride, which follows sodium in the metabolic sense, it is mainly excreted through the renal route. Re-uptake of chloride from the kidneys generally which follows the re-uptake of sodium. It is also excreted to sweat in some amount.

Potassium is excreted through the kidneys in a rate of 80-90%. The remaining portion is excreted through feces, and a very small amount is excreted through sweating. Potassium is filtered in the glomerules, reabsorbed in the proximal tubules and secreted in the distal tubules with Na-K exchange. Tubular secretion of potassium is affected from hydrogen ion exchange, acid-base balance and adrenal hormones.

Calcium is mainly excreted in the feces; it is excreted with sweat glands in small amounts.

Linearity/ nonlinear conditions:
POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION displays linear pharmacokinetic behavior if administered within the recommended dosage range.

5.3 Preclinical safety data
Since the components of the solutions are physiological components of the human and animal plasma, and since no toxic effects are expected from clinical administrations, no studies have been performed on POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION to evaluate its carcinogenic or mutagenic potentials and its effects on fertility.

Safety of the drugs added to the solution must be handled separately.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Water for injection
Hydrochloric acid

6.2 Incompatibilities
Compatibility of the drug to be added to the solution must be evaluated in advance. Any drug without compatibility data must not be added to the solution.

POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION must be used immediately after adding the compatible drug.

Decision of whether or not the added drug is compatible by checking any color change and/or precipitation, or presence compounds that have not been dissolved or crystallization are the responsibility of the doctor making the administration. The decision for the compatibility of the drug to be added to the solution must be made according to the instructions for use of the drug

and solubility and stability of the drug to be added to POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION at the pH of the solution (pH=4-6) must be confirmed before adding any drugs to the solution.

Some of the drugs incompatible with POLİFLEKS 5% DEXTROSE LACTATED RINGER SOLUTION FOR I.V. INFUSION is given below as a guide:

Some of the incompatible drugs:

- Amino caproic acid
- Amphotericin B
- Cortisone acetate
- Diethylstilbestrol
- Ethamivane
- Ethyl alcohol
- Solutions containing phosphate and carbonate
- Oxytetracycline
- Thiopental sodium
- Versenate disodium
- Ceftriaxone

Some of the partially incompatible drugs:

- Tetracycline is stable for 12 hours.
- 2%-3% solutions of ampicillin sodium are stable for 4 hours, while the solutions with concentrations higher than 3% are stable for 1 hour.
- Minocycline is stable for 12 hours.
- Doxycycline is stable for 6 hours

6.3. Shelf-life
24 months

Shelf-life during use: As regards microbiology, the drug must be used immediately after preparation for administration if the preparation procedure is not made under controlled and validated aseptic conditions. In cases where it is not used immediately, determining the conditions for and period of storage is the responsibility of the person who had added/diluted the drug.

6.4 Special precautions for storage
There are no special conditions for storage. It must be kept at room temperature under 25 °C.

6.5 Nature and contents of the container
In 100, 150, 250, 500 and 1000-ml PVC and PP bags. It has two forms, namely the forms with and without sets.

6.6 Destruction of the residual materials human medicinal product and other special precautions

The unused or waste products must be discarded according to the "Regulation Related to the Control of Medical Wastes" and the "Regulation Related to the Control of Packaging and Packaging Wastes".

Instructions for Use

The solution must be checked before use. **Only clear solutions not containing any particles within intact packaging must be used.**

With the purpose of preventing air embolism because of the residual air in the bag, serial connection to other infusion liquids must not be made.

The solution must be administered through the sterile application set using the aseptic technique. Fluid must be passed through the application set to prevent entry of air to the system.

Additional drug can be added with the help of an injector under aseptic conditions before or during the infusion. Isotonicity of the final products must have been determined before the parenteral administration.

The added drug must be mixed thoroughly before administering to the patient. Solutions containing additional drugs must be used immediately after the addition of the drug, and must not be kept to be used later.

Addition of drugs to the solution or erroneous application technique can cause febrile reaction depending on the contamination of the product with pyrogens. Infusion must be stopped immediately in case adverse reactions are seen.

It is for single use. **Partially used solutions must not be stored.**

Partially used bags must not be re-connected to systems applied to the patient.

How to open:

1. Check the intactness of the outer packaging and if there is any leakage; do not use the packaging if the packaging is damaged.
2. Tear off the protective outer packaging.
3. Check if the bag within the protective packaging is intact by squeezing the bag. Check the clarity of the solution within the bag and there is no foreign material within.

Preparations for the administration:

1. Hang the bag.
2. Remove the protective cap at the application tip.
3. Stab the spike of the application set to the application tip tightly.

4. The instructions of use of the set must be followed when administering the solution to the patient.

Addition of drugs

Caution: Like in all the parenteral solutions, all the substances to be added to the product must be compatible with the product. If any drug will be added to the product, compatibility must be checked before administration to the patient.

Adding drugs before administration:

1. The administration end will be disinfected.
2. The drug to be added will be added into the bag using and injector with a 19-22 gauge tip.
3. The solution with the added drug will be mixed thoroughly. For drugs with high density like potassium chloride, mixing will be ensured by tapping the application outlet of the bag gently when it is in the upside position).

Caution: Bags with added drugs must not be stored.

Addition of drugs during administration

1. The clamp of the set will be closed.
2. The administration end will be disinfected.
3. The drug to be added will be added into the bag using and injector with a 19-22 gauge tip.
4. Solution is removed from the hanger and turned upside down.
5. In this position, mixing of the added drug and the solution will be ensured by tapping the administration end and the injection input gently of the bag.
6. The bag will be brought to the previous position and administration will be continued.

7. MARKETING AUTHORISATION HOLDER

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