

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

PF IZOLEN BALANCED ELECTROLYTE SOLUTION FOR I.V. INFUSION

Sterile

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

#### Active ingredients:

Each 100 ml solution:

Sodium acetate trihydrate: 0.64 g

Sodium chloride: 0.50 g

Potassium chloride: 0.075 g

Sodium citrate dihydrate: 0.075 g

Calcium chloride dihydrate: 0.035 g

Magnesium chloride hexahydrate: 0.031 g

#### Excipients:

See section 6.1 for excipients.

### 3. PHARMACEUTICAL FORM

Sterile solution for intravenous infusion

### 4. CLINICAL PARTICULARS

#### 4.1 Therapeutical indications

PF IZOLEN BALANCED ELECTROLYTE is indicated for the treatment of water and electrolyte losses.

It is particularly preferred for patients in postoperative period, children with acute diarrhea and for prevention and treatment of the complications of the diabetic acidosis including dehydration, electrolyte imbalance (particularly hypokalsemia) and 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.

It is generally used 3 liters per 24 hours and one liter every 2-3 hours. The dosage in children with acute diarrhea and diabetic or renal acidosis and dehydration is 50-150 ml/kg.

##### Administration rate:

It will be administered as 120-240 ml per square meter of the body area.

**Route of administration:**

This solution is administered only through the intravenous route.

Administration will be made intravenously through sterile sets through peripheral or central veins.

With the purpose of minimizing the venous irritation during the peripheral administration of a hypertonic solution, the needle with the smallest diameter possible must be introduced to the largest vein possible, and infusion must be given with the slowest rate possible. Care must be taken to prevent the leakage of the administered fluid outside the vein.

See also section 6.6 for the details of the administration.

**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. However, since this drug is largely excreted through the kidneys, the risk of appearance of toxic effects will increase in cases where the renal functions are impaired. Therefore, care must be taken when selecting the dosage in renal failure (See: section 4.3).

**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.

It is generally recommended in the dosage range of 20-100 ml/kg /24 hours for this population.

**Geriatric population:**

Since the reduction of liver, kidney or cardiac functions is more frequent in the elderly population and possibilities of concomitant diseases or use of other drugs are more frequent in the elderly population, care must be taken in selecting dosage in this population, and the dose must be at the lower limit.

Since this drug is largely excreted through the kidneys, the risk of appearance of toxic effects will increase in cases where the renal functions are impaired. The reduction of renal functions is greater in the elderly; therefore, care must be taken in this population when selecting the dosage. Follow-up of the renal functions can be helpful in this population.

**Patients in postoperative period:**

The fluid-electrolyte requirements of the patients in the postoperative period must be calculated according to the daily electrolyte treatment principles. The following information can be used when calculating these requirements:

- When replacing the fluid loss, the contents of the fluid lost must be taken into consideration (gastric, gastrointestinal fistula, bile, small intestines, etc.), and suitable standard solutions must be selected or supplementing the solution with additional electrolytes, vitamins or minerals must be considered.
- The requirements of the patients must be calculated for each 24 hours.
- The formula "basal requirement + additional loss" will be used in calculations. The fluid amount calculated according to this formula will be divided into 3 equal portions and each portion must be administered through the intravenous route within periods of 8 hours.
- The basal fluid requirement is the amount of fluid and electrolytes required by a healthy individual within 24 hours under normal conditions. It can be calculated as follows:  
Adults: 35ml/kg (around 2500 ml in an adult weighing 70 kg)  
In infants and children:
  - 100 ml/kg for the first 10 kg of the body weight
  - 75 ml/kg for the second 10 kg of the body weight
  - 50 ml/kg for the third 10 kg of the body weight
- Basal electrolyte requirements is 1 mEq/kg/day for sodium and chloride (60-80 mEq in adults), and 0.5 mEq/kg/day for potassium (30-40 mEq in adults).
- The following information can be used in calculating the additional losses:  
The amounts of fluids taken and excreted by the patient must be calculated meticulously.

Long procedures in adults will require fluid transfusion of 10 ml/kg (500-700ml in the average) for each hour spent in the operation room.

It will be considered that an individual that had sweated in volumes enough to wet the bed sheets had lost at least 1 liter of fluid.

Nasogastric aspiration or fistula discharge fluids and urine must be collected for 24 hours.

Gauze soaked with blood, diarrhea diapers, and gauze used to dress the fistula area must be weighed and possible fluid content must be estimated.

Furthermore, the previous clinical experience and impressions must be taken into consideration.

#### **Patients with burns:**

Special formulas must be used for burns.

#### **4.3 Contraindications**

This solution is contra-indicated in anuria, severe oliguria, renal failure, crush syndrome, severe hemolysis, adrenal gland failure, hypoparathyroidism, cardiac block and high levels of plasma potassium.

This solution is contra-indicated also in alkalosis since it contains two-fold bicarbonate as compared to plasma. Plasma carbondioxide concentrations must be determined in patients that this solution is administered to.

#### **4.4 Special warnings and precautions for use**

Administration of intravenous solutions can cause fluid and/or solute overload that can result in dilution of serum electrolyte concentrations, over hydration, congestive conditions or pulmonary edema. The risk of dilution is inversely proportional with electrolyte concentrations.

The risk of congestive conditions that can result in peripheral or pulmonary edema is directly proportional with the electrolyte concentrations in the solution.

The ion concentrations of the solution and normal human plasma in mEq/liter (mmol/liter) are as follows:

	<b>IZOLEN BALANCED</b>	<b>PLASMA</b>
Sodium (Na <sup>+</sup> )	140 (140)	140 (140)
Chloride (Cl <sup>-</sup> )	103 (103)	103 (103)
Potassium (K <sup>+</sup> )	10 (10)	5 (5)
Calcium (Ca <sup>++</sup> )	4.8	4.8
Magnesium (Mg <sup>++</sup> )	3 (1.5)	3 (1.5)
Bicarbonate	-----	27 (27)
Acetate*	47 (47)	
Citrate*	7,65	

\* Bicarbonate precursors

Careful clinical observation is required at the beginning of all the intravenous infusions.

Administration must be implemented under regular and careful observation. Clinical and biologic parameters and particularly the serum electrolyte must be monitored.

Since the potassium level in the solution is two folds of the plasma, the solution must be administered slowly. The levels of carbon dioxide and potassium in the plasma must be determined, and electrocardiographic studies must be carried out. Potassium intoxication will not be seen if these precautions are taken. Additional potassium and lactate must be administered to the patient in case of severe hypokalemia and acidosis.

Since calcium chloride is tissue-irritant, intramuscular administration must be avoided and care must be taken to prevent leakage outside the vein in intravenous administration. Solutions containing calcium salts must be used carefully in patients with high levels of vitamin D like patients with impaired renal functions or with sarcoidosis. Furthermore, use in patients with renal calcium stones or patients with renal stones in their histories must be avoided. If blood transfusion will be made simultaneously, administration of PF IZOLEN BALANCED ELECTROLYTE through the same infusion system is not recommended because of the risk of coagulation by the calcium content.

Solutions containing sodium must be used with care in hypertension, cardiac failure, peripheral or pulmonary edema or in cases where the renal functions are impaired, in preeclampsia, aldosteronism or other conditions and treatments that have a course with sodium accumulation (e.g. corticosteroid therapy).

Solutions containing potassium salts must be used carefully in cardiac patients and in conditions creating predisposition to hyperkalemia including renal or adrenocortical insufficiency, acute dehydration excessive tissue destruction in severe burns.

With the purpose of minimizing the risk of incompatibility with any other 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 is the operation of the pump has been stopped before the complete emptying of the bottle; otherwise, air embolism can result.

The solution is administered intravenously through sterile sets. It is recommended that sets used for intravenous administrations will be replaced every 24 hours.

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

#### Warnings and precautions for pediatric use:

- The fluid and electrolyte balance of the neonates or very young infants can be affected from administration of very small volumes of fluids. Care must be taken in the treatment

of neonates and particularly the preterm neonates with immature renal functions and limited capability of excretion of fluids and solutes. Fluid intake, urinary output and serum electrolyte levels must be monitored closely.

Warnings and precautions related to is in geriatric patients:

- In general, the dosage must be selected carefully in the elderly. Considering that the liver, renal or cardiac functions may have been reduced in these patients, other drugs may be used concomitantly, or there may be co-morbidities accompanying the currently treated disease, it is recommended to start therapy with dosages in the lower limit of the dosage range.

Laboratory tests:

- Clinical evaluations and periodic laboratory tests must be performed to monitor changes in the fluid balance, electrolyte concentrations and acid-base balance in long-term parenteral administrations or whenever the status of the patient requires. Such values must be returned to normal with sodium chloride solutions containing dextrose or with alternative solutions when significant deviations from the normal values are seen.

**4.5 Interactions with other medical products and other modes of interaction**

Some drugs or other solutions can be incompatible with the solution. Like all the other parenteral solutions, compatibility with the added drugs must be evaluated by a doctor before use.

If other substances will be added to the solution, aseptic technique must be used and shaken till the substance is mixed. It must be made sure that there are no color changes, not dissolving particles or crystallization following the addition of drugs.

As regards the sodium contained in the solution, attention must be paid to the risk of sodium and water retention risk when using the solution together with corticosteroids and carbenoxolone.

Care must be taken when using the potassium-containing solutions with drugs that increase the potassium level in blood (potassium retaining solutions, ACE inhibitors, cyclosporine and drugs containing potassium salts like penicillin). PF IZOLEN BALANCED ELECTROLYTE has the potential of interaction with the following drugs in relation with the potassium it contains:

- Potassium retaining diuretics (amiloride, spironolactone or triamterene singly or in combination).
- Angiotensin converting enzyme inhibitors and possible angiotensin 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).

Calcium can increase the cardiac effect of digitalis and can cause digital intoxication. Hypocalcemia can occur if calcium salts are administered together with thiazides or vitamin D. Calcium salts reduce the absorption of bisphosphonate, fluoride, some fluoroquinones and tetracyclines. PF IZOLEN BALANCED ELECTROLYTE has the potential of interaction with the following drugs in relation with the calcium it contains:

- Digitalis group glycosides with effects that increase in the presence of calcium and can cause serious or fatal cardiac arrhythmias.
- Thiazide group diuretics or vitamin D that can cause hypercalcemia when administered together with calcium.

As a result of the sodium citrate and sodium acetate metabolism, alkalization of urine with bicarbonates will increase the renal clearance of acidic drugs including salicylic acid or barbiturates. Together with this, the half-lives of sympathomimetics and stimulants will increase and can cause toxicity.

#### **4.6 Pregnancy and lactation**

##### **General recommendations**

Pregnancy category: C.

##### **Women of childbearing potential /Contraception**

No data is available

##### **Pregnancy**

PF IZOLEN BALANCED ELECTROLYTE SOLUTION FOR IV INFUSION must not be used during pregnancy unless it is required for vitally important conditions.

There are insufficient data on the use of multiple electrolyte solutions in pregnant women.

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

Whether or not PF IZOLEN BALANCED ELECTROLYTE SOLUTION FOR IV INFUSION causes fetal damage if used in pregnant women, or if it causes impairment on ability of fertility

are not known. PF IZOLEN BALANCED ELECTROLYTE SOLUTION FOR IV INFUSION must be used in pregnant women only when it is absolutely necessary.

### **Lactation period**

It is not known whether or not this drug is excreted to human milk. Since it is known that many drugs are excreted to human milk, PF IZOLEN BALANCED ELECTROLYTE must be used carefully in breastfeeding mothers.

### **Reproductive ability / fertility**

Animal reproduction studies have not been carried out with solutions containing sodium chloride. No studies have been conducted for humans.

### **4.7 Effects on driving and using machines**

Driving is practically impossible during the use of solutions administered through infusion. It has no known effects on driving or use of machines.

### **4.8 Undesirable effects**

Adverse effects can be related to the deficiency or abundance of the ions and dextrose in the solutions; therefore, sodium and chloride levels must be monitored closely. Also, one should be cautious that additional drugs administered after diluting can cause adverse effects. In this case, the product characteristics of the additional drug must be referred to.

Infusion must be stopped upon any adverse effects seen during the administration, status of the patient must be evaluated and proper treatment measures must be taken.

The adverse effects reported in the clinical trials and after-marketing studies are listed according to the frequency order given below.

Very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ ), and unknown (available data do not allow deciding)

### **Blood and lymphatic system disorders**

Unknown: Acute hemolytic anemia (related to phosphorus deficiency)

### **Metabolism and nutrition disorders**

Unknown: Water retention and edema (related to hypernatremia); deterioration of congestive cardiac failure (related to hypernatremia); acidosis (related to hyperchloremia), deterioration of tissue oxygenation (related to phosphorus deficiency)

### **Psychiatric disorders**

Unknown: Hyperirritability, psychotic behaviors (related to hypomagnesemia)

### **Nervous system disorders**

Unknown: Mental confusion (related to hyperkalemia); reducing of the central nervous system functions (related to hypernatremia)

### **Cardiac disorders**

Unknown: Arrhythmias, cardiac block, electrocardiographic abnormalities, cardiac arrest (related to hyperkalemia); reducing of the cardiac functions (related to hypermagnesemia); Tachycardia (related to hypomagnesemia).

### **Vascular disorders**

Unknown: Hypotension (related to hyperkalemia); circulation collapse (related to hypermagnesemia); hypertension (related to hypomagnesemia).

### **Respiratory, thoracic and mediastinal disorders**

Unknown: Respiratory arrest (related to hyperkalemia); respiratory depression (related to hypermagnesemia).

### **Gastrointestinal disorders**

Unknown: Nausea, vomiting, diarrhea, abdominal cramps, diarrhea (related to potassium contained in the solution), Intestinal dilation and ileus (related to hypokalemia).

### **Skin and subcutaneous tissue disorders**

Unknown: Hot flush and sweating (related to hypermagnesemia).

### **Musculoskeletal and connective tissue disorders**

Unknown: Paresthesia in extremities, loss of reflexes, paralysis in extremities (related to hyperkalemia); deterioration of neuromuscular functions (related to hypokalemia); cramps, tetanus, hyperexcitability in muscles (related to phosphorus taken in excessive amounts as compared to calcium)

### **General disorders and related to the administration site**

Unknown: Fatigue (related to hyperkalemia);

### **Surgical and medical procedures**

Unknown: Febrile reactions; infection in the injection site; venous thrombosis or phlebitis starting the injection site and spreading; extravasation and hypervolemia

## **4.9 Overdose and treatment**

If fluid or electrolyte overload related to excessive infusion is seen during the parenteral treatment, the patient must be re-evaluated and proper corrective treatments must be started.

The adverse reactions related to the excessive sodium in the body include nausea, vomiting, diarrhea, abdominal cramps, thirst, decreases in the amounts of saliva, tear and sweat, fever, tachycardia, hypertension, renal failure, peripheral and pulmonary edema, respiratory arrest, headache, vertigo, restlessness, irritability, fatigue, muscular fasciculation and hardening, convulsions, coma and death.

Accumulation of excessive chloride in the body can cause bicarbonate loss and acidic shift in the body fluids.

Abnormally high levels of magnesium in plasma will cause hot flashes, sweating, hypotension, circulation collapse and decreases in the functions of heart and central nervous system. Respiratory depression threatens life.

Signs and symptoms of potassium intoxication include paresthesia in extremities, loss of reflexes, muscular or respiratory paralysis, mental confusion, fatigue, hypotension, arrhythmias, cardiac block, abnormalities in electrocardiograms and cardiac arrest.

Infusion must be stopped in case of overdose of solutions containing potassium, and the following measures will be taken to decrease potassium in serum:

- 10 or 25% dextrose solution in water with 10 units of crystallized insulin added for each 20 grams of dextrose will be administered with a rate of 300-500 ml per hour.
- Potassium absorption and exchange can be applied using sodium or ammonium cation exchange resins in the form of oral or retention enemas.
- Hemodialysis or peritoneal dialysis will be applied if required. Foods and drugs containing potassium must be stopped. However, it must be kept in mind that rapid lowering of the plasma potassium in digitalized patients can cause digital intoxication.

Administration of phosphorus replacement in excessive amounts can cause hypocalcemic tetanus.

Administration of phosphorus must always be accompanied by calcium support.

In case 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:** Intravenous solutions/ Solutions that affect the electrolyte balance

**ATC code:** B05BB02

PF IZOLEN BALANCED ELECTROLYTE is a sterile, stable and apyrogen solution intended for intravenous use. It includes no bacteriostatic substances.

Pharmacologic properties of the solution consists of the properties of its components (sodium, potassium, chloride, calcium, magnesium, citrate and acetate).

In the PF IZOLEN BALANCED ELECTROLYTE SOLUTION FOR IV INFUSION, sodium, chloride, calcium and magnesium concentration is the same with normal plasma, while potassium and bicarbonate equivalents (citrate and acetate) are two folds.

The basic effect of PF IZOLEN BALANCED ELECTROLYTE SOLUTION FOR IV INFUSION is the expansion of extracellular fluid compartment including the interstitial and intravascular compartments.

Potassium is the main cation of the intracellular fluid, and it is essential for the maintenance of the acid-base balance, isotonicity, and the electrodynamic characteristics of the cell. Potassium is important activator for many enzymatic reactions. Potassium is involved in the carbohydrate distribution and protein synthesis, gastric secretions, renal functions, transmission in nerves and muscular contractions (particularly in myocardium).

Sodium is the main cation of the extracellular fluid. It is involved in the distribution and balance of the fluids in the body. Changes seen in the body fluid volume are generally related to the loss of sodium from the body or retention of sodium in the body.

The organism attempts to preserve the fluid volume in the plasma and tonus by regulating the excretion of sodium with urine through the antidiuretic hormone secreted by the pituitary gland. In addition to this, sodium is an ion that plays a role in the protection of the acid-base balance in the body together with the chloride and bicarbonate ions.

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.

Chloride is the main anion of the extracellular fluid and its plasma levels are closely related to the sodium concentration. Changes in the chloride concentration are generally seen in the abnormalities of the sodium metabolism. Chloride is lost from the body together with sodium.

Magnesium is the main intracellular cation of the soft tissues, and is mainly involved in the enzymatic reactions of the carbohydrate and protein metabolism as a co-factor. Furthermore,

magnesium is also plays a role in the neurochemical transmission and neuromuscular excitability. Tachycardia, hypertension, over nervous sensibility and psychotic behaviors can be seen in magnesium deficiency.

Since acetate increases the blood pH and the total carbon dioxide in blood effectively, it is a bicarbonate precursor preferred in certain clinical conditions; it functions as a ready-to-use alkaline source for the body to be used in muscles and other peripheral tissues by being rapidly metabolized. Acetate enters the metabolic cycle at point from that of lactate, and requires less oxygen during the metabolism and formation of bicarbonate. This becomes particularly important in the existence of tissue hypoxia.

The electrolyte composition of the PF IZOLEN BALANCED ELECTROLYTE is more suitable for the prevention and treatment of dehydration in patients in postoperative period as compared to isotonic sodium chloride solutions, because this solution contains less sodium and chloride, and therefore, does not cause pathologic water and salt retention. Since the contained sodium, chloride, calcium and magnesium are in physiologic concentrations, electrolyte imbalance in the serum will be prevented. Its potassium content is twice the content in normal plasma; it removes the condition of negative potassium balance related to insufficient intake and surgical operations. The potassium level in the solution must not be considered as high; because a portion of this amount will be biochemically antagonized by the sodium and calcium in the solution, and even, administration of more potassium will be required in case of potassium deficiency. The amounts of citrate and acetate in the solution are equivalent to two folds of the bicarbonate amount in the normal plasma. The isotonic sodium chloride solutions do not have bicarbonate effect, moreover, they cause acidosis because of their chloride content. PF IZOLEN BALANCED ELECTROLYTE, however, corrects the medium-level acidosis and does not cause alkalosis.

Although isotonic sodium chloride solution causes fluid and salt retention, PF IZOLEN BALANCED ELECTROLYTE causes fluid and salt diuresis.

Dehydration, electrolyte imbalance (particularly hypokalsemia) and acidosis are seen frequently is proper measures are not taken in patients in postoperative period. PF IZOLEN BALANCED ELECTROLYTE is superior to isotonic sodium chloride solutions for the prevention and treatments of these complications seen in patients in postoperative period, children with acute diarrhea and diabetic acidosis.

## **5.2 Pharmacokinetic properties**

### **General properties**

Pharmacokinetic properties of PF IZOLEN BALANCED ELECTROLYTE consist of the properties of its components (sodium, potassium, chloride, calcium, magnesium, acetate and citrate).

### Absorption:

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

### Distribution:

Sodium distribution varies according to the tissues: it is fast in muscle, liver, kidney, cartilage and skin, slow in erythrocytes and neurons and very slow in bones.

Chloride is distributed mainly in the extracellular fluids.

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 the 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.

Magnesium is mainly distributed in the intracellular fluid (particularly within the soft tissue cells)

### Biotransformation:

The half-life following radioactive-labeled sodium ( $^{24}\text{Na}$ ) injection is 11 to 13 days for 99% of the injected sodium, and one year for the remaining 1%.

Chloride closely follows the sodium metabolism, and the changes in the acid-base balance of the body are reflected in the chloride concentration changes.

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.

Acetate, after being converted into acetyl-coenzyme A, which is the final carbon source of fat synthesis, is fully oxidized and metabolized in Krebs cycle. Since acetate ion is mainly metabolized in muscles and other peripheral tissues, has effective alkalizing effects even when the liver metabolism is impaired.

Acetate is infused to the organism as a sodium salt takes one hydrogen ion and gives one bicarbonate ion for each acetate ion consumed; then rapidly metabolized to carbon dioxide and water. Acetate ion is primarily metabolized in muscles and other peripheral tissues.

Changes of pH in the extracellular fluid 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.

#### Elimination:

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.

Chloride, which follows sodium in the metabolic sense, it is mainly excreted through the renal route.

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.

#### Linearity/ nonlinear conditions:

Electrolytes contained in PF IZOLEN BALANCED ELECTROLYTE display linear pharmacokinetic behavior if administered within the recommended dosage range, that is, in doses sufficient to supplement the deficiencies in the body.

When any drug is added to PF IZOLEN BALANCED ELECTROLYTE, the pharmacokinetics of these drugs will depend on the drug added.

### **5.3 Pre-clinic safety data**

Since the components of the solutions are physiological components of the human and animal plasma and no toxic effects are expected from clinical administrations, no studies have been performed on PF IZOLEN BALANCED ELECTROLYTE 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

### **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.

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 PF IZOLEN BALANCED ELECTROLYTE must be decided on by making use of the instructions for use of the drugs to be added to the solution.

Before adding any drug to the solution, it must be confirmed that the drug is soluble and stable at the pH of PF IZOLEN BALANCED ELECTROLYTE.

PF IZOLEN BALANCED ELECTROLYTE must be used immediately after the addition of any compatible drug.

Drugs known to be incompatible must not be added.

### **6.3. Shelf-life**

48 months

#### Shelf-life after addition of drugs:

- As regards microbiology, the drug must be used immediately after preparation for administration. 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; and this period is no longer than 24 hours under 2-8°C temperature if this procedure is not performed under validated aseptic conditions.

### **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 packaging**

500 and 1000-ml glass bottles

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”.

### Preparation for Use

The solution must be checked before use.

Administration is made intravenously through sterile sets.

### **Only clear solutions not containing any particles within intact packaging must be used.**

Administration must be started within the shortest time possible after attaching the application set to the product.

With the purpose of preventing air embolism because of the residual air in the bottle, 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 drugs can be added with the help of an injector under aseptic conditions before or during the infusion. Is tonicity 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 bottles must not be re-connected to systems applied 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 bottle using and injector with a 19-22 gauge tip.
3. The solution with the added drug will be mixed thoroughly.

**Caution:** Bottles 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 bottle using an 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 bottle.
6. The bottle will be brought to the previous position and administration will be continued.

## **7. MARKETING AUTHORISATION HOLDER**

POLİFARMA İLAÇ SAN. VE TİC. A.Ş.

Vakıflar OSB Mah. Sanayi Cad. No:22/1

Ergene/TEKİRDAĞ/TURKEY

Phone: +90 282 675 14 04

Fax: +90 282 675 14 05

## **8. MARKETING AUTHORISATION NUMBER(S)**

176/99

## **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date Of First Authorisation: 17.01.1996

Renewal Of The Authorisation: 24.02.2014

## **10. DATE OF REVISION OF THE TEXT**

30.09.2019