SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
PF 5% DEXTROSE-0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredients
Each 100 ml solution contains:
Dextrose monohydrate 5 g
Sodium chloride 0.9 g

Ionic concentrations of the solution:
- Sodium: 154 mEq/l
- Chloride: 154 mEq/l

Excipients:
See 6.1 for excipients.

3. PHARMACEUTICAL FORM
Sterile, apyrogen solution for intravenous infusion

4. CLINICAL PARTICULARS

4.1 Therapeutical indications
It is used in the treatment of conditions where the losses of sodium and chloride are less than the loss of water including vomiting, diarrhea, renal disorders or excessive use of diuretics as the source of fluid, electrolyte and carbohydrate.

It is also used in the preoperative and postoperative care as the initial hydration fluid that can meet the extracellular fluid losses and initiate the renal functions.

Together with the above, it is preferred in patients that fluids must be administered together with blood transfusion.

4.2 Posology and administration route
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 biological conditions (acid-base balance) and the concomitant treatments given.

In general, it is recommended in dosages of 500-3000 ml /24 hours for the adults, adolescents and elderly, and 20-100 ml/kg/24 hours for children, unless otherwise recommended by the doctor.

The frequency and dosage will be adjusted by the doctor according to the clinical conditions of the patient. The recommended infusion rate in adults and the elderly is 40 ml/kg per 24 hours and the recommended infusion rate in pediatric cases is 5 ml/kg per hour in the average (6-8 ml/kg in infants, 4-6 ml/kg in children between 1 and 6 years of age and 2-4 ml/kg in children older than 6 years of age).

With the purpose of preventing the development of hyperglycemia, the infusion rate must not exceed the glucose oxidation capacity of the patient. Therefore, the maximum glucose administration rate must be 500 to 800 mg/kg/hour.

Route of administration:
Administration will be made intravenously using sterile apyrogen sets.

Patients must be carefully monitored as regards urinary output and serum sodium and electrolyte concentrations during the administration of PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION.

Please see section 6.6 for details of 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.

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, and this dosage will be adjusted according to the body weight as follows.
0-10 kg: 100 ml/kg/day
10-20 kg: 1000 ml + 50 ml/day for each kg over 10 kg
> 20 kg: 1500 ml + 20 ml/day for each kg over 20 kg

Geriatric 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.

4.3 Contraindications
This solution is contra-indicated in patients who administration of sodium or chloride will be clinically harmful.

- Hypervolemia
-Hypernatremia
-Hyperkalemia
-Heart Failure
-Acute Ischemic Stroke
-Lactic acidose
-General Edema and ascites with cyirosis
-Pediatric patients with kidney, liver or heart failure
-In the first 24 Hours after head trauma
-Diabetes under control

Solutions containing dextrose are contra-indicated in patients with hypersensitivity against products containing corn.

4.4 Warnings and precautions related to special uses
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.

The solution includes 154 mmol/l sodium (Na^+) and 154 mmol/l chloride (Cl^-); osmolarity is about 585 mOsm/l.

Solutions containing sodium must be used carefully in patients with congestive cardiac insufficiency, serious renal failure or sodium retention together with edema. Administration of solutions containing sodium ions can cause sodium retention in patients with reduced renal functions.

Over administration of solutions not containing potassium can cause significant hypokalemia. Serum potassium levels must be maintained in normal levels and potassium must be added to the solution if needed.

Precautions:
This solution must be administered carefully in conditions of hypervolemia, renal failure, and obstruction of urinary tracts, potential cardiac failure or overt cardiac insufficiency.

Administration of additional electrolytes can be needed in excessive nasogastric irrigation, vomiting, diarrhea or drainage from gastrointestinal fistulas.

Essential electrolytes, minerals and vitamins must also be added to the treatment where required.

Sodium-containing solutions must be administered carefully in patients taking corticosteroids or corticotropins or who have salt retention with other reasons. In cases with renal or cardiovascular insufficiency accompanied or not accompanied by congestive heart failure, particularly in the postoperative period or in the elderly, sodium-containing solutions must be used carefully.

Solutions containing dextrose must be administered carefully in patients known to be diabetic as well as those with subclinical diabetes or in those with carbohydrate intolerance with any reason.

Hypokalemia can develop during the parenteral use of hypertonic dextrose solutions. Dextrose solutions must be used by adding potassium in sufficient amount in fasting patients with good renal functions particularly is the patient is under treatment with digitalis-type drugs.

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 is the operation of the pump has been stopped before the complete emptying of the bag; 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.

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.

Warning and precautions for pediatric use:
Effectiveness and reliability of dextrose solutions containing sodium chloride have not been shown in duly designed controlled studies carried out on pediatric patients.

Dextrose is effective and reliable in the pediatric patients in the stated indications (See: Indications). It has been stated in the literature that intravenous dextrose dosage and administration rate must be adjusted carefully in pediatric patients and particularly in the neonates and infants with low birth weights because of the increased risk of hyper-/hypoglycemia. The serum glucose concentrations must be monitored closely in pediatric patients and particularly in the neonates and infants with low birth weights.

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 (See: "Warnings" and "Posology and route of administration").

Warnings and precautions related to is in geriatric patients:
In the clinical studies carried out with dextrose solutions containing sodium chloride, individuals 65 years old or older have not been included to allow determining if the elderly respond differently as compared to young adults. Based on the other clinical experiences reported, no differences were found in the responses of the elderly and the young adults.

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.

These drugs are largely excreted through the kidneys, and therefore, the risk of toxic reaction increases in patients with impaired renal functions.

Since reducing of renal functions is more frequent in the elderly than in the young adults, care must be taken in selecting the dosage in the elderly patients (See: "Warnings" section).

4.5 Interactions with other medical products and other modes of interaction

Solutions containing sodium can cause sodium and water retention (edema and hypertension) in patients taking corticosteroids or carbenoxolone.

Solutions containing dextrose must not be administered together with blood transfusion if they do not contain electrolytes in adequate amounts, this can cause hemolysis and erythrocyte agglomeration.

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.

PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION must not be used during pregnancy unless it is required for vitally important conditions.

Pregnancy
Studies on animal reproduction with dextrose solutions containing sodium chloride have not been carried out.

Whether or not PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE 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. PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION must be used in pregnant women only when it is absolutely necessary.

Labor:
Effects of PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION on the labor, effects on labor with forceps or other interventions, and the effects on other interventions required on the neonate together with the effects on growth, development and functional maturity of the infant when used during labor are not known.

It has been reported in the literature that solutions containing dextrose and saline have been used during labor. It must be considered when required by the fluid balances of the mother and fetus, glucose or electrolyte concentrations and acid-base balance, or when required by the conditions of the mother or fetus.

Lactation
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 5% DEXTROSE - 0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION must be used carefully in breastfeeding mothers.

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.

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥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)

Metabolic and nutritional disorders
Unknown: Water retention and edema; deterioration of congestive cardiac failure (related to hypernatremia); acidosis (related to hyperchloremia), fluid and electrolyte imbalance*; Hyperglycemia and dehydration**

Nervous system disorders
Unknown: Headache, vertigo, uneasiness, irritability, convulsions, coma and death (related to hypernatremia).

Cardiac disorders
Unknown: Tachycardia (related to hypernatremia).

Vascular disorders
Unknown: Hypertension (related to hypernatremia).

Respiratory, thoracic and mediastinal disorders
Unknown: Pulmonary edema, respiratory depression and respiratory arrest (related to hypernatremia).

Gastrointestinal disorders
Unknown: Nausea, vomiting, diarrhea, abdominal cramps, thirst, and reducing the saliva amount (related to hypernatremia).

Skin and subcutaneous disorders
Unknown: Reducing of sweating (related to hypernatremia).

Musculoskeletal and connective tissue disorders
Unknown: Fasciculation and hardening of muscles (related to hypernatremia).

Renal and urinary disorders
Unknown**:** Renal failure (related to hypernatremia), polyuria

General disorders and administration site conditions
Unknown: Fever; fatigue (related to hypernatremia)

Surgical and medical procedures***
Unknown: Febrile reactions; infection in the injection site; local pain or irritation; venous irritation; venous thrombosis or phlebitis starting the injection site and spreading; extravasation and hypervolemia

* Including hypokalemia, hypomagnesemia or hypophosphatemia
** Adverse effects generally seen as a result of erroneous parenteral administration
*** Adverse effects that can be seen as a result of application technique

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 bottle must be kept for examination if needed.

4.9 Overdose and treatment

If fluid or solute loading due to excessive infusion is observed during parenteral treatment, the patient should be re-evaluated and appropriate corrective treatments should be initiated.

In cases where sodium intake is impaired by the kidneys, extra sodium retention can cause pulmonary and peripheral edema. When sodium chloride is given in therapeutic doses, hypematremia rarely occurs. The most serious effect of hypematremia is drowsiness and confusion, leading to brain dehydration, which can later progress to convulsions, coma, respiratory failure and death. Other symptoms include thirst, saliva and decreased tear secretion, fever, tachycardia, hypertension, headache, dizziness/dizziness, restlessness, irritability, and weakness.
Overdosing of chloride-containing salts can lead to a loss of bicarbonate, causing an acylating effect.
Prolonged or rapid administration of isosmotic solutions containing dextrose can cause edema and water intoxication.
Prolonged or rapid administration of solutions containing dextrose can cause hyperglycemia and, accordingly, hyperosmolarity, dehydration, hyperglycosuria and osmotic diuresis.,

If the dose is accidentally exceeded during treatment, administration should be discontinued and the patient should be monitored for signs and symptoms associated with the drug administered. If necessary, symptomatic and supportive treatments should be applied for these symptoms.

5. PHARMACOLOGICAL PROPERTIES

Pharmacodynamic and pharmacokinetic characteristics of PF 5% DEXTROSE - 0.9 % SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION is related to glucose, sodium and chloride contained.

5.1 Pharmacodynamic properties

Pharmacotherapeutical group: Solutions affecting the electrolyte balance/Electrolyte solutions containing carbohydrates
ATC code: B05BB02

Ions like sodium pass through the cellular membrane using various transport mechanisms include sodium pump (Na-K-ATPase). Sodium plays an important role in neurotransmission, cardiac electrophysiology and renal metabolism.

Chloride is mainly an extracellular anion. Intracellular chloride is found in high concentration in red blood cells and in the gastric mucosa. Reuptake of chloride follows the reuptake of sodium.

Glucose is the main energy source in the cellular metabolism. 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.

Sodium chloride solutions containing carbohydrates have been developed with the purpose of replacing the fluid and electrolyte deficiencies in the body and meeting some part of the energy requirement. Such solutions have beneficial effects when chloride loss is equal to or greater than the loss of sodium because of sweating, vomiting or gastric aspiration.

Furthermore, administration of blood and dextrose solutions not containing electrolytes to the patients through the two branches of a Y-type intravenous infusion device will cause pseudo-agglutination of erythrocytes. Although this agglutination may not cause hemolysis, it can result in transfusion reactions. Some amount of electrolytes must be added to the solution to eliminate this incompatibility with blood and aqueous dextrose solutions. Five percent dextrose solutions containing 0.9% sodium chloride can be administered together with blood.

5.2 Pharmacokinetic properties

General properties

Pharmacokinetic properties of PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION consist of the properties of its components (dextrose, sodium and chloride).

Absorption:

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

Distribution:

Glucose can be administered with dosages up to 0.5 g/kg per hour without causing glucosuria. Approximately 95% of the glucose administered with the rate of 0.8g/kg, which is the highest administration rate will remain within the body.

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.

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.

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%.

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

Elimination:
Carbon dioxide forming as a result of the biotransformation of glucose is excreted via the lungs, while water is mainly excreted through the kidneys, and through sweat, feces and expiration air in small amounts.

Sodium is excreted mainly through the renal route; however, majority is absorbed back with the renal route. A small amount of sodium is excreted through feces and sweat.

Since chloride follows sodium in the metabolic sense, it is mainly excreted through the renal route, and with feces and sweat in small amounts.

Linearity/ nonlinear conditions:
The electrolytes and glucose in the composition of PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION display linear pharmacokinetic behavior if administered in rates adequate for the supplementation of the deficiencies in the body, that is, in therapeutical dosages.

5.3 Pre-clinic 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 PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE 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

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.

Solubility and stability of the drug at the pH of PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION must be confirmed before adding the drug to the solution.

Some of the drugs incompatible with PF 5% DEXTROSE - 0.9% SODIUM CHLORIDE SOLUTION FOR I.V. INFUSION:

- Ampicilin sodium
- Mitomycin
- Amphotericin B
- Erythromicin lactobinate

Drugs known to be incompatible must not be added to the solution.

6.3 Shelf life

24 months

6.4 Special precautions for storage

There are no special conditions for storage. It must be kept at room temperature under 25 °C away from direct light.

6.5 Nature and contents of the packaging

In 500 and 1000-ml glass bottles.
It has two 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 local regulations!

Details for use:

Solution should be inspected visually before use.
The administration is by intravenous route with sterile, apyrogen sets.

Only products that are clear, particle-free and intact in packaging integrity should be used.

The administration should be started as soon as possible after the application set is attached to the product.

In order to prevent an air embolisation that may occur due to the residual air in the bottle, no serial connection should be made with other infusion fluids.

The solution should be applied using the aseptic technique through the sterile application set. In order to prevent air from entering the system, liquid must be passed through the application set before use.

Additional medication may be added before and during infusion with the aid of Injection a needle in aseptic conditions. The final product's isotonicity should be determined before parenteral administration.

The added drug must be completely mixed with the solution before application to the patient. Solvents containing additional drug should be used immediately after drug addition; it should not be stored for later use.

Addition of additive or wrong application technique may result in a fever reaction due to pyrogen contamination of the product. If an adverse reaction occurs, the infusion should be terminated immediately.

For single use only.
Do not store partly used solutions.
Do not reconnect partly used bottles to the administration systems.

Addition of additional drug:
Attention: As with all parenteral solutions, all substances to be added to the product must be compatible with the product. If an addition is to be made, compatibility should be checked in the final mixture before administration to the patient.

Adding medication before administration
1. Stopper of the bottle is disinfected.
2. Inject the drug to be added to the bottle by using syringe with 19 to 22 gauge needle.
3. Mix the solution and the added drug thoroughly.

Attention: Do not store the bottles which mixed with additional medication.

Adding medication during administration
1. Close the clamp.
2. Stopper of the bottle is disinfected.
3. Inject the drug to be added using syringe with 19 to 22 gauge needle.
4. Remove the solution from the hanger and invert.
5. In this position, tap gently the bottle to allow mixing of solution and medication.
6. Return the bottle to its former position and open the clamp and continue administration.

7. MARKETING AUTHORISATION HOLDER
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