SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT
POLİFLEKS 60 mg/ml Dextran 70 9 mg/ml Isotonic Sodium Chloride Solution for I.V. Infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active ingredients:
In each 100 ml solution:
Dextran: 70 g
Sodium chloride: 0.9 g

Excipients:
See section 6.1 for excipients.

3. PHARMACEUTICAL FORM
Solution for infusion,
It is a colorless, clear, sterile and apyrogen solution without particle. Osmolality is 308.86 mOsm/L. Electrolyte concentrations are sodium 154 mEq/L and chloride 154 mEq/L.

4. CLINICAL PARTICULARS
4.1. Therapeutic indications
It is used in the prophylaxis and treatment of shocks based on surgeries and other traumas, bleeding or burns, for preventing the thromboembolic caused by traumas. Furthermore, it provides protection from postoperative thrombosis and lung emboli.

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

Adults
Dextran 70 isotonic solution is used as intravenous infusion.

In shock: when dextran 70 isotonic solution is used as an addition to the other varieties of shock treatment, the dosing and infusion depend on the amount of liquid loss and final hemoconcentration and must be determined based on the needs of the patient. The total dosage of the 6% solution must not be over 1.2 g/kg (20 mL/kg) during the first 24 hours. If the treatment time exceeds 24 hours the daily dosage must not be over 0.6 g/kg (10 mL/kg). The routing dose for adults is 30 g (500 mL). In emergencies the medicine may be administered to adults with a speed of 1.2 – 2.4 g (20 – 40 mL) per minute. For the patients who are normovolemic or close to normovolemic, infusion speed must not be over 0.24 g (4 mL). Dextran 70 must not be administered subcutaneously.

Rate of administration:
In emergencies the medicine may be administered to adults with a speed of 1.2 – 2.4 g (20 – 40 mL) per minute. For the patients who are normovolemic or close to normovolemic, infusion speed must not be over 0.24 g (4 mL).

Route of administration:
This solution is used only through intravenous route.
Administration is made through intravenous route from peripheral or central veins by means of sterile apyrogen sets.

During the administration of a hypertonic solution through peripheral route, in order to minimize venous irritation possibility, the needle with the smallest lumen must be located to the widest vein as much as possible; infusion must be made in the slowest way possible. Care must be given that the liquid administered leaked out of vein.

Special populations:
Renal/ hepatic impairment
When using dextran in cases of shocks of the patients who have heart and renal failure, congestive heart failure and lung edema threat must be taken into consideration. It must not be used for the kidney patients who severe oliguria and anuria are dominant. It must not be used for the patients who have apparent cardiac disorder.

Paediatric population
There is no adequate clinical study related with children. It may be administered by calculating the dose based on body weight for children.

Geriatric population
Since decrease in the liver, kidney or cardiac functions is seen more and the probability of seeing other diseases simultaneously or using other medicine is higher, in general the dose selection for the elderly must be made with care and by generally taking the lowest limit possible of the dose range.

Since there is no adequate study on elderly, a dosing different from the anticipated is not in question.

4.3. Contraindications
For the people who have excessive sensitivity against dextran, it is contraindicated in all kinds (thrombocytopenia and hypofibrinogenemia etc.) including the things made by some medicines, in apparent cardiac failure, in kidney patients with severe oliguria and anuria, in hypervolemia conditions, in severe bleeding diseases, in cases where sodium and chloride may be clinically harmful.

4.4. Special warnings and precautions for use

This solution may cause excessive loading in the circulation; therefore it must be used with care for the patients' renal function of who is damaged. There is the risk of developing pulmonary edema and congestive heart failure.

Administration of intravenous solutions may cause dilution in the serum electrolyte concentration, severe hydration, liquid and/or solute loading such that congestive conditions or pulmonary edema occurs. Dilution risk is inversely proportional to the electrolyte concentration. The risk that congestive conditions which may cause peripheral and pulmonary edema develop is directly proportional with the electrolyte concentration in the solution.

A careful clinical monitoring is required at the start of all intravenous infusions. Administrations must be conducted under a regular and careful surveillance. Clinical and biological parameters, especially serum electrolyte levels must be monitored.

It may hinder platelet function (especially at a dose of about 15 ml/kg), therefore it must be used with care for the patients who have thrombocytopenia.

The bleeding time may temporarily extend for the patients who take dextran 70 more than 1 liter (or with a dose of approximately 15 ml/kg). Besides, a slight increase may be seen in bleeding tendency.

Dextran 70 causes an apparent decrease in factor VIII and a decrease more than expected in the hemodilution effects at factor V and IX. It forms generally in doses close to 15 ml/kg. Care must be given for the trauma and serious surgical patients who the early indications of bleeding complications may be seen. Blood loss may slightly increase in the post-operative patients.

Hematocrit may be seen after the administration of dextran 70. It must be avoided that the volume decreases below 30%.

It may increase the probability of Rouleaux formation; blood samples must be taken for typology and cross-matching before dextran infusion. Maintain the samples, if it is required for the later usages.

Administration of dextran solutions with big volume may result in decreased plasma protein concentration.

Each 500 ml solution contains 6% dextran 70 and 0.9% sodium chloride. This sodium chloride provides 77 mEq sodium.

The products containing sodium ion must be used with care for the patients who severe renal failure, congestive heart failure and edema formed due to the sodium retention are seen.

General warnings, precautions and contraindications related with sodium chloride and dextran 70 must be taken into consideration.

Vomiting and involuntary defecation may occur in the patients under anesthesia. It must be used carefully in pathologic abdominal conditions and for the patients who had ongoing intestinal surgery.

Hypersensitivity reactions may be seen (Urticarial, nasal congestion, sneezing, pressure in chest, hypotension). These effects may be decreased by using antihistaminic.

Rarely, severe, anaphylactic reactions induced by dextran were announced (such as urticarial, sneezing, pressure in chest, hypotension, nausea and vomiting, shock, heart and respiratory standstill, and death). It is seen even with very small doses typically at the commencement period of the infusion in the patients to whom dextran 70 administration wasn't made previously. The patients to whom dextran 70 administration wasn't made previously must be closely followed up especially at the first minutes of the infusion.

In the event that allergic reaction symptoms are seen, stop dextran 70 administration. Take medical precautions immediately (parenteral epinephrine, antihistaminic or other supporting treatments). If the circulation collapses because of anaphylactic shock even though dextran 70 usage is stopped, the administration is started rapidly with another agent increasing volume.

Administering 20 ml of dextran 70 before dextran 70 infusion decreases the probability of anaphylactic reaction occurrence however in spite of this, serious reactions may happen.

Keep resuscitation precautions ready during dextran usage.

Infection at the point of injection, venous thrombosis or phlebitis starting at the injection point, hypervolemia, and febrile reactions may occur during IV administration of dextran 70. If this kind of reactions occurs, don't continue infusion, evaluate the patient, take the necessary therapeutic counter measures and save the remaining solution, if it will be necessary, for the tests.

It must be used with care in the diabetic patients.

Dextran must be used with care in the patients suffering from impaired renal clearance. Loading may happen in the circulation. Besides, there is the sodium retention risk in the patients having renal failure.

If you meet allergic reactions such as labored breathing, swelling in face, tongue, lips, or neck, urticarial, take medical aid urgently. If you face with sneezing or pressure in the chest, urinating less or never, swelling in the foots and hands, extraordinary bleeding or non-stopping bleeding, lightheadedness, burning, itching, swelling or pain feeling in the injection region, absolutely tell

this to your physician. You may see less severe side effects such as nausea, vomiting, stomach ache, slight itching, rush in the skin, joint ache, and nasal congestion.

For the patients having heart and renal failure, the danger of heart failure and lung edema must be taken into account when using dextran in shock condition. There may be patients who are extremely sensitive to dextran, like for all chemicals. Allergic reactions (urticarial, nausea, vomiting) may be seen very rarely during the infusion of dextran solutions. Antihistaminic medicines, ephedrine and adrenaline remove these reactions in a short time. Dextran 70 administration must be stopped in the patients having reaction.

4.5. Interaction with other medicinal products and other forms of interaction

For not causing erroneous results, the samples must be taken before the treatment for determining cross-matching, Rh and blood type and some of the samples must be stored for more advance evaluations to be made during the treatment. Saline agglutination and indirect antiglobulin methods can be used for additional blood samples, cross-matching and blood type determinations after the commencement of infusion while using proteolytic enzyme techniques for cross-matching test may cause difficulties. Blood glucose determinations made by using sulfuric acid or acetic acid hydrolysis after the administration of dextran 70 isotonic solution may give high values and the laboratory tests made by using turbidimetric measurements in the serum may be seen higher than normal. The blood samples for these tests must be taken before starting dextran 70 isotonic solution infusion. Hemorrhage risk is in question in case that it is given together with heparin.

Dextran may cause turbidity in the bilirubin amount determination made by using alcohol and total protein amount determination tests made by using biuret and therefore may cause problems in the amount determination.

Care must be given to the IV treatments for sodium in the corticosteroid and corticotrophin tests.

Some medicines and solutions added to the solution may be incompatible. If other materials will be added to the solution, aseptic method must be used and it must be rinsed until it mixes completely. The medicine to be used in parenteral route, before the administration, must be inspected for having foreign substances inside or color changes as much as the solution and package allow.

Additional information related with special populations

No interaction study was made.

Pediatric population:

No interaction study was made.

4.6. Pregnancy and lactation

General advice

Pregnancy category: C.

Women of childbearing potential /Contraception

There is no known adverse effect.

Pregnancy

It is not known whether the substances contained by the solution are harmful for the fetus when administered to pregnant women or not or affect the reproduction capacity or not; because of this it must not be administered to pregnant women unless it is very necessary.

Lactation

There is no adequate information on the migration of dextran to breast milk. Because it is formulated together with sodium chloride and nutrition with breast milk with high sodium content may cause neonatal hypernatremia dehydration, it must not be used during lactation period, unless it is very necessary.

Reproduction ability / fertility

It has no effect on reproduction ability/fertility.

4.7. Effects on ability to drive and use machines

It is not practically possible to use vehicles during the usage of the solutions administered through infusion. There is no known effect on vehicle and machine usage after it is used.

4.8. Undesirable effects

Undesirable effects may be cause by the lack or excess of ions in the solution. Therefore it is required that electrolyte levels are closely monitored. Besides, eye must be kept open that the additional medicines administered by diluting may cause adverse effects too. In such a case, the product information of the additional medicine must be checked. When a side effect is seen during administration, the infusion must be stopped, the condition of the patient must be evaluated and suitable treatment measurements must be taken.

The adverse effects reported in the clinic studies and the studies after marketing are listed based on frequency levels below:

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), unknown (it cannot be progressed with the data on hand).

Metabolism and nutrition disorders

Very rare: Hypernatremia

Vascular disorders

Rare: fleabite, leakage outside the vein, hypervolemia

Very rare: venous thrombosis

Gastrointestinal disorders
Unknown: Nausea, vomit

Musculoskeletal and connective tissue disorders
Unknown: Arthralgia.

General disorders and administration site conditions
Very rare: fever reactions, infection in the injection area

4.9. Overdose and treatment
When an excessive loading based on liquid or solutes is seen in the patient during parenteral treatment, the condition of the patient is evaluated and corrective treatment methods are applied.

5. PHARMACOLOGICAL PARTICULARS

5.1 Pharmacodynamics properties

Pharmacotherapy group: ones used instead of blood and plasma protein fractions
ATC code: B05AA05

Dextran 70 isotonic sodium chloride solution is a glucose polymer with a high molecular weight, the average molecular weight of which is 70 000. The main links in the polymer are 1-6 glycoside type links. It is synthesized through fermentation with the effect of Leuconostoc menensteroides strains on the sucrose. Dextran 70 isotonic sodium chloride solution is similar to human serum albumin for pharmacological effects and molecular weight. Following the intravenous administration, the main effect of the Dextran 70 isotonic sodium chloride solution is the plasma volume widening caused by the colloidal osmotic effect of the medicine by attracting the liquid to the intravascular cavities from the interstitial cavities. Dextran 70 isotonic sodium chloride solution forms a plasma volume widening slightly bigger than the volume of the solution infused. Maximum plasma volume widening is reached about one hour after the end of the infusion. The level and time of the widening in the plasma volume range depending on the volume of Dextran 70 isotonic sodium chloride solution infused and depend on the plasma volume before the administration and renal clearance speed of the dextran.

5.2. Pharmacokinetic properties

General properties
The pharmacokinetic properties of this solution consist of the properties of the components.

Absorption: Since it is a product administered parenteral, it is evaluated that absorption is complete.

Distribution: Dextran 70 is distributed only to the plasma compartment. The distribution volume, because of this, is equal to the plasma volume.

Biotransformation: The molecules with a molecular weight over 50000 split into glucose slowly and glucose is metabolized by converting into water by carbon dioxide.

Elimination: Most of it is eliminated without turning into urine within 24 hours. A small part is eliminated with feces.

5.3. Pre-clinic reliability data
No study was made about whether the active ingredients contained in the composition of polifleks dextran 70 isotonic sodium chloride solution have mutagenic, teratogenic, and carcinogenic effects or not.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Water for injection

6.2. Incompatibilities
The incompatibility of the medicine to be added to the solution must be evaluated beforehand. In cases where there is no incompatibility data, no medicine must be added to the solution.
If other materials will be added to the solution, aseptic method must be used and rinsed until it is mixed. The medicines to be used in parenteral route must be inspected for having foreign substances inside or for the color changes as much as the solution and package allow.

6.3. Shelf-life
36 months.

6.4. Special precautions for storage
If the solution is not clear and contains particles or if the bag is damaged it must not be used.

Store in room temperature less than 25°C.

It must be used immediately after it is opened. The remaining part of the solution some of which is used must not be used.

6.5. Nature and contents of the container
Polifleks dextran 70 isotonic sodium chloride solution is presented inside PVC bags of 500 ml and 1000 ml.

6.6. Destruction of the residual materials human medicinal product and other special precautions
Unused products or waste materials must be disposed according to the “regulation for controlling medical wastes” and “regulation for controlling packages and package wastes”.

Preparation for the administration:

A) The bag is turned upside down several times for the twist-off bag is wetted.
B) The twist-off cap of the bag is twisted and removed.
C) The clamp setting the number of drops on the infusion set is closed.
D) The protector on the spike of the infusion set (the part perforating the plastic) is removed by twisting to left and right. The spike is inserted to the center of the twist-off cap.
E) It is squeezed until the dropping chamber is half filled and released. The protector in the needle tip is removed. Clamp is opened and perfusion system and needle is filled with solution. The clamp is closed and the vein is entered. Then, clamp is opened and number of drops is adjusted.

7. MARKETING AUTHORISATION HOLDER
POLİFARMA İLAÇ SAN. VE TİC. A.Ş.
Vakıflar OSB Mah. Sanayi Cad. No:22/1
Ergene/TEKİRDAĞ/TURKEY
Tel : +90 282 675 14 04
Fax : +90 282 675 14 05

8. MARKETING AUTHORISATION NUMBER(S)
208/77

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Date Of First Authorisation: 04.09.2006
Renewal Of The Authorisation:

10. DATE OF REVISION OF THE TEXT
15.09.2018