SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

LİFE-EXTEND 60 mg/ml dextran 70 + 75 mg/ml sodium chloride solution for I.V. infusion
Sterile

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:
Each 100 ml of solution contains;

Dextran 70	6g
Sodium Chloride	7.5 g

pH:3.5-7.0

Excipients:
For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Sterile solution for intravenous infusion.
Clear solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

LİFE-EXTEND, is used in the initial treatment of hypovolaemia with hypotension induced by traumatic injury.

4.2 Posology and method of administration

Posology/frequency and duration of administration

LİFE-EXTEND is administered as a single 250 ml dose intravenously, as the initial treatment after primary stabilisation of respiration and bleeding.
LİFE-EXTEND should be given by rapid i.v. infusion (a full dose in 2-5 minutes).
Treatment with LİFE-EXTEND should be followed by immediate administration of isotonic fluids, dosed according to the needs of the patient.

Method of administration:
The application is done intravenously with sterile sets.

Additional information on special populations:

Renal/Hepatic failure:
It should not be used in patients with renal failure.
Since there is no specific study for patients with hepatic failure, there is no specific dosage recommendation for this group patients.

Pediatric population:
Since there are no studies specific to this population, there is no specific study for this group of patients.There are no dosage recommendations.

Geriatric population:
Since there are no studies specific to this population, there is no specific study for this group of patients.There are no dosage recommendations.

4.3 Contraindications

- It is contraindicated in people with hypersensitivity to dextran 70 and sodium chloride.
- It is contraindicated in pregnancies close to birth.

4.4 Special warnings and precautions for use

Attention should be paid to haemostatic competence in patients on concomitant treatment with drugs known to affect coagulation. The amount of dextran 70 (15 g) contained in LİFE-EXTEND will not affect haemostasis, since changes in haemostatic variables only occur at doses above 1.5 g dextran /kg bodyweight. Aggressive fluid resuscitation can, however, dilute blood clotting factors to such an extent that a bleeding diathesis occurs.

As LİFE-EXTEND is a potent volume expander, caution should be exercised in patients with compromised cardiac function

In patients with diabetes having severe hyperglycaemia with hyperosmolality, hypertonic solutions should be used with caution. If this condition is known or suspected other forms of fluid treatment should be considered.

Infusion of hypertonic sodium chloride without colloid in patients with chronic renal failure has been observed to cause clinically relevant hyperkalemia.

Pretreatment with hapten dextran (Promit, Promiten) has been shown to reduce the risk of hypersensitivity reactions during dextran usage. In the clinical trials performed to this dextran 70-sodium chloride mixture for the initial treatment of trauma induced hypotension, no such pretreatment was given. Depending on the acuteness of the shock state preinjection of hapten

dextran, when available, should be considered and the potentially higher risk for anaphylactic reactions in case hapten dextran is not used should be weighed against the benefit to the patient

This medicinal product contains 7.37 g sodium per 250 ml. This should be considered for patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction
There is no known interaction, but see. Section 4.4

4.6 Pregnancy and lactation

General recommendation
Pregnancy category: C

Women with childbearing potential/Contraception
There is no data available.

Pregnancy

There is no clinical experience with LİFE-EXTEND during pregnancy. In animal studies, effects on the foetus have been observed with dextran 70 (see 5.3). The relevance of these data for humans is unknown.
Anaphylactic reactions in the mother in connection with parturition have been observed to cause anoxia in the foetus. Foetal death and neurological sequelae has occurred in connection with the use of infusion fluids containing dextran 40 without pre-injection of hapten dextran. LİFE-EXTEND should therefore not be administered to pregnant women at term or in association with delivery.

Lactation
It is not known whether this drug passes into breast milk. In view of the active substances, its use in lactating mothers is not considered to pose any risk to the child.

4.7 Effects on ability to drive and use machines
It is not available.

4.8 Undesirable effects
Adverse effects reported in patients during clinical trials and post-marketing experience are listed below. The frequency classification of reported adverse drug reactions is as follows:

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); Not known (cannot be estimated from the available data)

No undesirable effects have been attributed to LİFE-EXTEND in the clinical trauma trials. Local pain close to the site of infusion has been observed in healthy volunteers. It was attenuated by gentle massage distal to the infusion site. See Section 4.4 regarding the risk for anaphylactic reactions to dextrans and the use of hapten dextran.

4.9 Overdose and therapy
Not applicable. LİFE-EXTEND is administered as a single dose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Blood substitutes and plasma protein fraction
ATC Code: B05AA05
Both dextran 70 and sodium chloride contribute to the effect of LİFE-EXTEND on intravascular volume. Water, primarily from the intracellular compartment, is rapidly shifted into the vascular compartment by the hypertonic component, 7.5% NaCl. The effect of the hypertonic component subsides rapidly due to extravasation of sodium and chloride. The dextran component remains in the circulation for much longer and contributes to a prolonged duration of the volume effect. The increase of intravascular volume provided by 250 ml of LİFE-EXTEND has been found to be 2 to 3 times the infused volume, similar to the increase in volume resulting from intravenous administration of 3 liters of crystalloid solution. Statistically significant overall survival benefit of LİFE-EXTEND compared to standard of care was not demonstrated in the clinical trials. In subgroup analyses treatment benefits were observed for patients with severe injuries such as penetrating injury requiring surgery and for patients requiring intensive care.

5.2 Pharmacokinetic properties

General properties:
The pharmacokinetic properties of sodium chloride and dextran 70, respectively, are not affected by simultaneous infusion. After infusion of this dextran 70-sodium chloride mixture, plasma sodium increases by 9 to 12 mmol returning to normal in less than 4 hours. Dextran 70 has a plasma half-life of 6 to 8 hours. Dextran molecules below the threshold for glomerular filtration (molecular size less than 50 000 D) are excreted in the urine unaltered while larger molecules are taken up by the RES where they are degraded to glucose by endogenous dextranases.

5.3 Preclinical safety data
In acute and subacute toxicology studies of its active components, doses 4 to 5 times the clinical dose, on a body weight basis, have resulted in toxic effects such as disorientation, inactivity, vomiting, increased salivation and a few cases of lethality, mainly due to the hypertonic sodium chloride component. In studies in pregnant rabbits and mice in which 6% dextran 70 was administered during the period of organogenesis, delayed ossification was observed in the

foetuses of both species after daily doses 2 and 6 times higher than that contained in one unit of solution to man. In mice there was also an increase in the incidence of exencephaly. It is not known whether the hypertonic component could enhance this effect. There are no studies covering the last trimester of gestation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients
Water for injection

6.2 Incompatibilities
In the absence of incompatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf Life
24 months

6.4 Special precautions for storage
There is no special precautions for storage. Store at room temperature below 25°C.

6.5 Nature and contents of container
250 ml PP bags without set.

6.6 Special precautions for disposal and other handling

Unused products or waste materials should be disposed of in accordance with the "Medical Waste Control Regulation" and "Packaging and Packaging Waste Control Regulation". Only clear, particle-free and intact packaging integrity products should be used. The solution should be checked before use. The application is done intravenously with sterile sets. Application should be started as soon as possible after the application set is attached to the product. Serial connections with other infusion fluids should not be made to prevent an air embolism that may occur due to residual air in the bag. The solution should be applied using a aseptic technique through a sterile administration set. Liquid must be passed through the application set before use to prevent air from entering the system. It is disposable. Partially used solutions should not be stored. Partially used bags should not be reconnected to the systems applied to the patient.

To open:

1. Check the strength of the outer packaging and for leaks; do not use if the packaging is damaged.
2. Tear open the protective outer packaging.
3. Tightly check whether the bag in the protective packaging is intact. Check the clarity of the solution in the bag and whether it contains foreign matter.

Application preparations:
1. Hang the bag.
2. Remove the protective cap on the application tip.
3. Insert the spike of the application set firmly into the application tip.
4. The instructions for use of the set should be followed to apply the solution to the patient.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

2019/30

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 21.01.2019
Date of renewal of the authorization:

10. DATE OF REVISION OF THE TEXT