SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

CARDİPASSİVE cardioplegic solution for cardiac perfusion
Sterile

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active Substance:
Each 1000 ml:

Sodium chloride	6430 mg
Calcium chloride dehydrate	176 mg
Magnesium chloride hexahydrate	3253 mg
Potassium chloride	1193 mg

Electrolyte concentrations:

Sodium:	110 mmol/L
Chloride:	160 mmol/L
Magnesium:	16 mmol/L
Calcium:	1,20 mmol/L
Potaissum:	16 mmol/L

Excipient(s):

Sodium hydroxide	q.s

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

Cardioplegic solution
Colorless, clear solution.

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

CARDIPASSIVE is used in combination with ischemia and hypothermia when properly buffered, to provide cardiac arrest through direct intracardiac infusion to the isolated vascular bed during open heart surgery.

4.2. Posology and method of administration

Posology/frequency and duration of administration
CARDİPASSİVE should be used only by those trained to perform open heart surgery
The following information is recommended as a guide and may change depending on the surgeon's preferences and experience.

For pH adjustment, 10 ml (840mg) (10 mEq of sodium and bicarbonate from each of sodium and bicarbonate) should be aseptically added to each 1000 ml cardioplegic solution. When

measured at room temperature, use 10 ml of 8.4% Sodium Bicarbonate Injectable Solution to obtain an approximate pH value of 7.8. Since the pH of Sodium Bicarbonate Injectable Solutions is variable, this pH may not be obtained with another Sodium Bicarbonate Injectable Solution.

Adding sodium bicarbonate should be done just before application, since it is not stable with other compounds. After this procedure, the solution should be used within 24 hours. The solution should be cooled to 4°C before use.

After the formation of the cardiopulmonary bypass at 28°C-30°C perfusate temperatures and cross clamping of the ascending aorta, the buffered solution is applied to the aortic root by the rapid infusion method. The infusion start rate can be 300 ml/m^2/min over a period of 2-4 minutes. (Approximately 540 ml/min in an adult with a surface area of 1.8 m^2 and a height of 1.73 m and 70 kilos)

Simultaneous external cooling (regional hypothermia of the pericardium) can be achieved by cooling a physiological solution such as NormosolR-R (balanced electrolyte replacement solution) or USP Ringer's Injectable solution to 4°C and delivering it into the chest cavity.

If myocardial electromechanical activity persists or reappears, the solution can be infused again at a rate of 300 ml/m^2/min over a 2-minute period. Solution infusions may be repeated more frequently every 20-30 minutes or if myocardial temperature rises above 15°C-20°C or if cardiac activity is observed to return.

The amount of solution applied to the aortic root may vary depending on the type or duration of the open heart surgery procedure

Method of administration:
It is administered intracardiacly.
CARDIPASSIVE is applied by rapid infusion to the aortic root after adding sodium bicarbonate (10 ml of 8.4% solution for 1000 ml CARDIPASSIVE solution) and after cooling to 4°C.

Additional information on special populations
Renal failure:
No information.

Hepatic failure:
No information.

Pediatric population
The safety and efficacy of CARDIPASSIVE has not been established in pediatric patients. Clinical myocardial protection strategies and cardioplegic solutions that are effective in the adult heart may be less effective in the immature heart due to differences in structure, function and metabolism.

Geriatric population:
In general, caution should be exercised in the selection of an elderly patient, and the dose range should generally be started at a low level, reflecting a decrease in liver, kidney and cardiac functions, as well as a high frequency of concomitant diseases.

CARDIPASSIVE is a unique product due to its excretion through the liver or kidneys and no special dosage adjustment is known for the elderly.

4.3. Contraindications

-In patients known to be hypersensitive to CARDIPASSIVE or any of the excipients,
-CARDIPASSIVE should not be used without adding sodium bicarbonate.
-CARDIPASSIVE is not suitable for intravenous administration.
-If the solution is not clear or its packaging is damaged, do not apply CARDIPASSIVE. Discard any unused parts.

4.4. Special warnings and precautions for use

CARDIPASSIVE is only used for open heart surgery during cardiopulmonary by-pass surgery where the coronary circulation is isolated from the systemic circulation.

Magnesium and potassium plasma rates may increase if CARDIPASSIVE is used in larger volumes to allow it to pass through the extracorporeal circulation and penetrate into the general circulation secondarily. Severe hypotension and metabolic acidosis have been reported when large volumes (8-10 liters) of cardioplegic solution are allowed to enter the pump and systemic circulation during bypass. It is recommended that CARDIPASSIVE be discharged from the right ventricle in case of large volume use. It should not be used without adding a suitable buffer such as sodium bicarbonate to 8.4%.

Following the addition of the buffer, CARDIPASSIVE should be cooled to 4°C and used within 24 hours before use.

To maintain hypothermia, myocardial temperature must be monitored throughout the operation. Continuous electrocardiograms can be applied to detect changes in myocardial activity throughout the operation.

Appropriate equipment that can be used immediately should be available for a possible heart defibrillation that may be required following cardioplegia.

Inotropic drugs should be available in the postoperative period.

The CARDIPASSIVE bag should not be used in series-connected applications.

This medicinal product contains 110 mmol sodium per 1000 ml. This should be considered for

patients on a controlled sodium diet.

This medicinal product contains 16 mmol potassium per 1000 ml. This should be considered for patients with reduced kidney function or patients on a controlled potassium diet.

4.5. Interaction with other medicinal products and other forms of interaction
There may be incompatibility with concomitant medications.

Additional drugs should be added according to the aseptic technique and should be mixed thoroughly. The resulting solution should not be stored.

4.6. Pregnancy and Lactation
General Advice
Pregnancy category: C

Women with childbearing potential / Contraception
There is not sufficient data on use of CARDİPASSİVE in pregnant women.

Pregnancy
There are no studies that determine the effect of CARDIPASSIVE, animal reproduction or fetal development in humans. CARDIPASSIVE should not be used during pregnancy unless necessary.

Lactation
No information.

Reproduction ability / Fertility
No information.

4.7. Effects on ability to drive and use machines
No effect of CARDIPASSIVE on the ability to drive and use machines has been reported.

4.8. Undesirable effects
Side effects are natural conditions for open heart surgery, such as myocardial infarction, electrocardiotic abnormalities, and arrhythmias (irregularities in the heart rhythm), including ventricular fibrillation. Spontaneous healing may be delayed or not realized after cardioplegic cardiac arrest when switching to normal circulation. Defibrillation with electroshock may be required to restore heart functions.

4.9. Overdose and therapy
Excessive administration of CARDIPASSIVE solution may cause unnecessary dilatation of the myocardial vascular system, as well as a leak in the perivascular myocardium, which may cause tissue edema.
In case of overdose, symptomatic treatment should be started.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Solutions affecting electrolyte balance
ATC Code: B05BB01

Mechanism of action
The application of CARDIPASSIVE by sodium bicarbonate after cooling and adding it to the coronary vascular system by dropping provides rapid stopping of the contractile activity in the myocardium in open heart surgeries and storing energy stocks.

CARDIPASSIVE reduces the negative effects of metabolic acidosis and myocardial ischemia, fights losses of intracellular ions. This solution provides surgeons with a good working condition by providing a bleeding-free surgical field, easy access, a calm and relaxed heart. Application of this solution allows the heart functions to recover quickly after surgery.

The high concentration of potassium ion (K^+) is responsible for the rapid arrest of the electromechanical activity of the heart. Rapid cessation of cardiac activity provides the preservation of the energy required for the resumption of contractile activity after ischemia.

Sodium (Na^+) and Chloride (Cl^-) ions do not play a specific role in stopping the heart. Sodium is important to maintain the ionic integrity of myocardial tissue. Chlorine ions are necessary to maintain the electrolytic neutrality of the preparation.

The low concentration calcium ion (Ca^{++}) contained in the cardioplegic solution maintains the integrity of the cell membrane in order to prevent the appearance of the calcium paradox during reperfusion.

Magnesium ion (Mg^{++}) helps stabilize the myocardial membrane by inhibiting myosin phosphorylase, which preserves ATP reserves for the recovery of postischemic activity.

The addition of bicarbonate ion (HCO_3^-) allows the solution to be buffered and slightly alkaline to compensate metabolic acidosis that accompanies ischemia.

5.2. Pharmacokinetic properties

General properties
No information.

5.3. Preclinical safety data

No information.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Sodium hydroxide
Hydrochloric acid
Water for injection

6.2. Incompatibilities

Since incompatibility studies are not available, this drug should not be mixed with other drugs.

6.3. Shelf-life

24 months

6.4. Special precautions for storage

Store at room temperature under 25°C.

The solution prepared by adding 10 ml of 8.4% sodium bicarbonate is stable for 24 hours at 4°C.

6.5. Nature and contents of container

1000 ml PP bag.

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".

Important note:

As mentioned above (See Section 4.4), the CARDIPASSIVE bag should not be used in series-attached applications.

Parenteral products should be inspected for particulate matter and discoloration prior to administration.

To open:
Tear outer wrap at notch and remove solution bag. To add 10 ml of 8.4% sodium bicarbonate solution and the necessary medicines, follow directions below before preparing for administration.

To Add Medication:

1. Prepare additive port for medicine.
2. Using aseptic technique and an appropriate needle, hole diaphragm and inject. Withdraw needle after injection.
3. The additive port may be protected by covering with an additive cap.
4. Mix bag contents thoroughly.

Preparation for Administration

1. Close flow control clamp of administration set.

2. Remove cover from outlet port at bottom of CARDİPASSİVE bag.
3. Insert piercing pin of administration set into port with a twisting motion until the set is firmly seated.
Note: In case of using a purified administration set, replace the antibacterial filter with the cannula protective cap.
4. Suspend container from hanger.
5. Squeeze and release drip chamber to establish proper fluid level in chamber.
6. Attach aortic infusion device to set
7. Open flow control clamp to expel air from set and aortic infusion device. Close clam
8. Position aortic infusion device to introduce solution into aortic root.
9. Regulate rate of administration with flow control clamp

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

2019/99

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21.02.2019
Date of renewal of the authorisation:

10. DATE OF REVISION OF THE TEXT

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