**sp.zn. sukls30351/2023**

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE MEDICINAL PRODUCT

**Solutio Thomas cum procaino Ardeapharma** concentrate for solution for infusion

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1000 ml of the concentrate for infusion solution contains:

| | |
|---|---|
| Magnesii chloridum hexahydricum | 162.65 g |
| Kalii chloridum | 59.60 g |
| Procaini hydrochloridum | 13.60 g |
| pH of the solution | 3.2 - 4.5 |
| Osmotic pressure | 6 200 kPa |

Excipient with a known effect: sodium disulphite

For the full list of excipients, see the section 6.1.

## 3. PHARMACEUTICAL FORM

Concentrate for solution for infusion

Description of the preparation: clear, no more than slightly yellowish solution

## 4. CLINICAL PARTICULARS

### 4.1. Therapeutic indications

Induction of cardioplegia in combination with hypothermia during open heart surgery using extracorporeal circulation. The product is intended for adult and adolescent patients.

### 4.2. Posology and method of administration

40 ml of Thomas solution is removed aseptically, then added into 1000 ml of Ringer solution, which is pre-chilled to 4 °C, and the mixture is blended. Then actual acidity of the mixture is adjusted to pH value of 7.8 by aseptic adding of approximately 5-10 ml of infusion solution of sodium hydrogen carbonate with 84 g/l concentration. With regard to varied actual acidity of Ringer solutions from different producers, it is important to check pH value of each individual mixture prepared.

The solution prepared as above contains 152.1-157.1 mmol of $Na^+$, 36 mmol of $K^+$, 32 mmol of $Mg^{2+}$**,** 2.3 mmol of $Ca^{2+}$, 253.6 mmol of $Cl^-$, 4-10 mmol of $HCO_3^-$, 2 mmol of procainii in 1045 – 1050 ml.

After extracorporeal circulation having been linked up, activated and a transverse clip applied on aorta ascendens, the solution diluted, adjusted and pre-chilled to 4 °C as given above is applied via rapid infusion into coronary circulation. The initial dose usually is 300 ml/$m^2$ administered during about 1 minute, which means 540 ml within 1 minute in adult patient (weighing 70 kg). Continuous external cooling of pericardium is performed by instillation of Ringer solution pre-chilled to 4 °C. If electro-mechanic activity of myocardium persists, then, 2 minutes after, additional 300 ml/$m^2$ in the course of 1 minute can be administered. The application is possible to be repeated in 20-30 minutes, alternatively even sooner, namely when the myocardium temperature is in range of 15-20 °C and a return of myocardium activity is observed.

Total volume of undiluted product administered can vary depending on the type and duration of the surgery.

### 4.3. Contraindications

Hypersensitivity to procaine. Others are given by contraindications for open heart surgery.

### 4.4.Special warnings and precautions for use

The product of Solutio Thomas cum procaino Ardeapharma can be used only after the dilution by Ringer infusion solution and the adjustment of actual acidity (see the dosage); the further condition for use is the solution temperature of 4 °C. It can be used exclusively during extracorporeal circulation when the coronary circulation is isolated from the system circulation.

Thomas solution must not be used for any other therapeutic purpose except from cardioplegia induction, not even after its dilution.

The product contains sodium bisulphite that can cause severe allergic reactions and bronchospasm.

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

Procaine contained in the product causes an increase in effectivity and toxicity of antiarrhythmic drugs, muscle relaxants or vasodilators.

### 4.6.Fertility, pregnancy and lactation

The use of the product during pregnancy and lactation is not contraindicated if the patient´s condition requires such use.

### 4.7.Effects on ability to drive and use machines

With regard to the character of the product and its indication is not relevant.

### 4.8.Undesirable effects

After use of major volume of the product, an increase in $Mg^{2+}$ and $K^{+}$ plasma levels can occur. With the administration of 8-10 litres of diluted product, hypotension and metabolic acidosis can occur. The overdose by the product can also cause dilation of coronary circulation or even myocardium oedema. In case of hypersensitivity to procaine, anaphylactic shock can develop.

**Reporting of suspected adverse reactions**

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the address:

Státní ústav pro kontrolu léčiv (State Institute for Drug Control)
Šrobárova 48
100 41 Praha 10

Website: www.sukl.cz/nahlasit-nezadouci-ucinek

### 4.9.Overdose

After use of major volume of the product, an increase in $Mg^{2+}$ and $K^{+}$ plasma levels can occur. With the administration of 8-10 litres of diluted product, hypotension and metabolic acidosis can occur. The overdose by the product can also cause dilation of coronary circulation or even myocardium oedema.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1.Pharmacodynamic properties

Pharmacotherapeutic group: cardioplegia solutions, varium, ATC code: B05XA16

$K^{+}$ ions in the concentration used cause an immediate stop of electric activity of the myocardium and that is why a reserve of energy is maintained. $Mg^{2+}$ ions help to maintain the myocardium membrane integrity by inhibition of the phosphorylase acting on myosin that protects ATP reserves. The action of $K^{+}$ and $Mg^{2+}$ ions appears to have an additive effect on preservation of energy for post-ischemic activity. $Ca^{2+}$ ions (contained in Ringer solution) prevent the formation of deviation of calcium content in

myocardial cell membrane. $HCO_3^-$ ions ensure an adequate adjustment of actual acidity of the diluted product and this way they compensate the inception of metabolic acidosis. $Na^+$ ions are necessary for maintenance of composition of the content in myocardial cells. $Na^+$ ions do not play any specific role in cardioplegic effect of the product equally as $Cl^-$ ions that only sustain electroneutral proportion of the product. Procaine chloride decreases the irritability of myocardium, decreases the possibility of arrhythmia and has a vasodilation effect on coronary arteries.

### 5.2.Pharmacokinetic properties

Cardioplegic solution applied via rapid infusion into coronary circulation is after the restoration of coronary circulation washed out of the heart into blood circulation. Procaine is after resorption hydrolysed by cholinesterase into para-aminobenzoic acid and diethylaminoethanol. Para-aminobenzoic acid is in 80 % eliminated by urine while diethylaminoethanol in 30 %, the remaining part is metabolized in the liver. Ionic components of the solution are eliminated by urine.

### 5.3.Preclinical safety data

With regard to the composition and use of the product were not worked out.

## 6. PHARMACEUTIAL PARTICULARS

### 6.1.List of excipients

Sodium disulphite

Solution of hydrochloric acid 1 mol/l

Water for injections

### 6.2.Incompatibilities

With regard to the fact that the product must not be used for any other purpose except for cardioplegia induction, the use of other substances is not expected with the exception of those given above in the section “Posology and method of administration“.

### 6.3.Shelf life

4 months provided that the package is intact.

The shelf life after the first opening:

Chemical and physical stability before the use after the opening was confirmed for 48 hours at 25°C.

From microbiological point of view, the product should be used immediately. If it is not used immediately, then the period and storage conditions of the product after the opening before the use are within the reliability of the user and in common case it should not be longer than 24 hours
at 2-8 °C as far as the opening/dilution was not performed under the controlled and validated aseptic conditions.

### 6.4.Special precautions for storage

Store the infusion bottle in the box to protect the product from light. Protect from frost.

### 6.5.Nature and contents of container

Infusion glass bottle with a rubber stopper and an aluminous closure, carton box.

Package size: 1x 50 ml, 20x 50 ml

Not all package sizes may be marketed.

### 6.6. Special precautions for use, disposal and other handling

This medicinal product is dispensed entirely on the base of medical prescription.

**The product is not intended for direct use, it must be diluted before the administration!**

40 ml of Thomas solution is removed aseptically, then added into 1000 ml of Ringer solution, which is pre-chilled to 4 °C, and the mixture is blended. Then actual acidity of the mixture is adjusted to pH value of 7.8 by aseptic adding of about 5-10 ml of 84 g/l infusion solution of sodium hydrogen carbonate.

With regard to varied actual acidity of Ringer solutions from different producers, it is important to check pH value of each individual mixture prepared.

The solution prepared as above contains 152.1-157.1 mmol of $Na^+$, 36 mmol of $K^+$, 32 mmol of $Mg^{2+}$**,** 2.3 mmol of $Ca^{2+}$, 253.6 mmol of $Cl^-$, 4-10 mmol of $HCO_3^-$, 2 mmol of procainii in 1045 - 1050 ml.

After extracorporeal circulation having been linked up, activated and a transverse clip applied on aorta ascendens, the solution diluted, adjusted and pre-chilled to 4 °C as given above is applied via rapid infusion into coronary circulation.

For accurate dosage and method of administration, see the section 4.2.

Use the solution only when it is clear, without visible particles and the package is intact.

The product must not be applied repeatedly; it is intended for a single use.

Any unused product or waste should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER

ARDEAPHARMA, a.s., Třeboňská 229, 373 63 Ševětín, Česká republika (Czech Republic)

## 8. MARKETING AUTHORISATION NUMBER(S)EGISTRAČNÍ ČÍSLO

41/029/01-C

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

Date of the first authorisation: 24th January 2001

Date of the last renewal of the authorization: 13th November 2013

## 10. DATE OF REVISION OF THE TEXT

27th March 2023