

## PRODUCT INFORMATION

### *RCH Monosodium L-aspartate 14mmol/10mL ampoule*

## NAME OF THE MEDICINE

RCH Monosodium L-aspartate 14mmol in 10mL Concentrated Injection

## DESCRIPTION

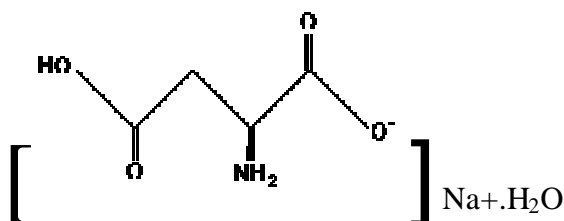
RCH Monosodium L-aspartate is a sterile, clear, colourless solution, containing monosodium aspartate 14mmolL (added as the monohydrate) and water for injections to 10.0 mL. The pH of the solution is 7.3 to 7.6.

**Synonyms:** L-aspartic acid sodium salt monohydrate, asparaginic acid sodium, asparaginic acid sodium salt

**Chemical formula:**  $C_4H_6NNaO_4.H_2O$

Molecular mass: 101.10 for monosodium aspartate monohydrate (98.09 for anhydrous monosodium aspartate)

**Chemical structure:**



**CAS:** 3792-50-5 for monosodium aspartate monohydrate

**CAS:** 56-84-8 for anhydrous monosodium aspartate

Monosodium aspartate monohydrate exists as a white crystalline powder. It is soluble in water.

## PHARMACOLOGY

During cardiac surgery, the use of cardioplegia solution, usually in combination with cardiac hypothermia, produces rapid and complete diastolic arrest. Cardioplegia solution is used to minimise myocardial energy requirements and prevent ischaemic damage which may be caused by the absence of coronary blood flow during the arrest phase. Cardioplegia solution also minimises or prevents reperfusion injury when coronary blood flow is restored.

Aspartate, when used as an additive to cardioplegia solution, may protect myocytes during ischaemia by increasing anaerobic energy production.

RCH Monosodium L-aspartate is added to cardioplegia solutions prior to use in cardiac surgery. It is not intended for use alone. (*See Dosage and Administration*).

***Pharmacokinetics:***

RCH Monosodium L-aspartate, as an additive to cardioplegia solutions, should not be absorbed systemically if the correct procedures are followed. However, if large volumes of diluted cardioplegia solution are instilled and allowed to return to the heart lung machine without venting from the right heart, systemic absorption is possible.

No pharmacokinetic studies specific to RCH Monosodium L-aspartate are available.

**CLINICAL TRIALS**

Several published studies are available in the clinical literature to support the use of monosodium aspartate as an additive to cardioplegia solutions. RCH Monosodium L-aspartate solution was not employed in any of these studies.

There were five randomised controlled trials enrolling a total of 209 patients undergoing cardiopulmonary bypass surgery, with or without left ventricular dysfunction. The concentration of L-aspartate added to the cardioplegia solution was 13 mmol/L in most studies. The 5 trials used either warm or cold (or both) blood cardioplegia for the various stages of cardioplegia (induction, maintenance, reperfusion) rather than crystalloid cardioplegia.

While findings varied due to a variety of possible factors including different techniques, composition of cardioplegia solutions and clinical status of patients, the consensus is that a beneficial effect of aspartate has been demonstrated usually in the immediate post cardiopulmonary bypass period rather than in the longer term.

In one non-randomised study of donor heart preservation techniques in 62 transplant patients, aspartate enhancement of initial crystalloid cardioplegia used to arrest donor hearts and subsequent controlled reperfusion after implantation lead to an increased incidence of spontaneous defibrillation and a trend towards lower inotrope requirements.

**INDICATIONS**

Substrate for organ perfusion.

**CONTRAINDICATIONS**

RCH Monosodium L-aspartate must not be administered as a single agent into the patient, but only as an additive to cardioplegia solution.

RCH Monosodium L-aspartate is contra-indicated in patients with a prior hypersensitivity to aspartate.

**PRECAUTIONS**

RCH Monosodium L-aspartate is used as an additive to cardioplegia solutions. It must be used only by specialists trained in cardiac perfusion techniques and open heart surgery. Inotropic support drugs and appropriate defibrillation equipment should be readily available following the use of cardioplegia solutions.

RCH Monosodium L-aspartate must not be administered by direct intravenous injection and must be mixed with cardioplegia solution prior to use. The subsequent admixture is used only for instillation to the coronary arteries when the coronary circulation is isolated from the systemic circulation during cardiopulmonary bypass.

Caution should be taken to avoid inadvertent release of aspartate into the systemic circulation by venting of the right heart during cardiopulmonary bypass. Systemic absorption is unlikely in the hands of experienced perfusionists and surgeons

Monosodium aspartate is an excitatory neurotransmitter, with the ability to stimulate NMDA receptors in the brain. Caution should be taken in the event that the cardioplegia solution inadvertently reaches the general circulation.

***Carcinogenicity, genotoxicity and effects on fertility:***

Monosodium aspartate is the sodium salt of aspartic acid, a nonessential amino acid. As an additive to cardioplegia solutions, monosodium aspartate is unlikely to be carcinogenic or genotoxic or to affect fertility.

***Use in pregnancy:***

Australian Pregnancy Category B2

The potential effects of monosodium aspartate on embryofetal development have not been investigated in animal studies. Its effect upon the human fetus has not been established. It should be administered to pregnant women only if unavoidable.

***Use in lactation:*** Due to lack of data, use of monosodium aspartate solution in breastfeeding women is not recommended.

***Interactions with other medicines***

Systemic absorption of cardioplegia solutions containing monosodium aspartate should not occur if recommendations for use are followed; therefore interactions between the cardioplegia solution and other medicines are unlikely unless large volumes of cardioplegia solution enter the systemic circulation. This could result in elevations of sodium, potassium and other constituents of the cardioplegia solution, as well as aspartate levels.

Interactions of aspartate with any ingredients of cardioplegia solutions, or with other drugs, have not been reported in cardioplegia procedures.

**ADVERSE EFFECTS**

Any adverse effects reported during cardioplegia procedures are generally related to the procedures, as cardiac surgery is associated with intraoperative and peri-operative risks, including myocardial infarction, ECG abnormalities and arrhythmias.

Cardioplegia solutions may cause electrolyte and acid-base abnormalities (e.g hyperkalaemia) but no adverse effects in several published randomised controlled trials have been attributed solely to aspartate as an additive.

Patients undergoing cardiac surgery should be closely monitored for any adverse effects.

## **DOSAGE AND ADMINISTRATION**

A final concentration of 14mmol/L monosodium aspartate in blood is achieved by adding 20mL (28mmol) of monosodium aspartate and 30mL of 8.4% sodium bicarbonate to a 500mL bag of cardioplegia solution from which 50mL has been removed and discarded. The resulting solution is diluted at a ratio of 1 in 3 with blood to give a monosodium aspartate concentration of 28mmol in 2L (14mmol/L).

The admixture is prepared immediately prior to commencement of cardioplegia and is maintained at room temperature (18 – 25°C) for the duration of the procedure (up to 6 hours). During the bypass procedure, the solution temperature is adjusted via the heat exchanger on the bypass circuit to 32°C until arrest, then reduced to 24°C for the remainder of the induction dose.

Common constituents of cardioplegia solutions include: sodium, potassium, magnesium, chloride, glucose, lidocaine; sodium bicarbonate is also added to the cardioplegia solution at the time of addition of monosodium aspartate.

RCH Monosodium L-aspartate contains no antimicrobial agent. The reconstituted product should be used immediately. The product is for treatment of one patient only on one occasion. Discard any remaining contents

*Note: RCH Monosodium L-aspartate is intended for use as an additive to cardioplegia solutions. The instructions for administration for specific cardioplegia solutions should be consulted prior to use.*

*RCH Monosodium Laspartate is not suitable for admixture with Cardoplegia 'A' Solution (Baxter Healthcare Pty Ltd) or DBL Sterile Cardioplegia Concentrate (Hospira Pty Ltd).*

***RCH Monosodium L-aspartate should not be given as a direct intravenous infusion.***

## **OVERDOSAGE**

Overuse of cardioplegia solution may lead to excessive dilatation of coronary vessels and leakage into the perivascular myocardium, possibly causing tissue oedema. Any adverse effects should be treated symptomatically. If large volumes of cardioplegia solution enter the systemic solution, elevations of sodium, potassium and other constituents of the cardioplegia solution may occur, however this situation is unlikely in the hands of experienced perfusionists and surgeons.

In case of overdose, immediately contact the Poisons Information Centre for advice on 131126.

## **PRESENTATION AND STORAGE**

RCH Monosodium L-aspartate is supplied in a 10mL ampoule containing 14mmol/10mL monosodium aspartate for single use only. It is available in packs of 5 x 10mL ampoules.

The product contains no preservative and is intended for use in one procedure only. Any remaining solution should be discarded.

*Storage:* Store below 30°C. Protect from light.

## **SPONSOR:**

The Royal Children's Hospital  
Pharmacy Department,  
Flemington Road,  
Parkville VIC 3052

## **POISON SCHEDULE:**

Not scheduled

**AUST R No: 54264**

**Date of TGA approval:** 13<sup>th</sup> October 2011