1 CARDIOPLEGIA SOLUTION A (solution)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1000mL contains the following active substances:

Sodium chloride B.P.	6.43g
Potassium chloride B.P.	1.19g
Magnesium chloride hexahydrate B.P.	3.25g
Calcium chloride dihydrate B.P.	176mg

The mixture contains the following ions in 1000mL:

Sodium	110mmol
Magnesium	16mmol
Chloride	160mmol
Potassium	16mmol
Calcium	1.2mmol

For the full list of excipients, see Section 6.1.

3 PHARMACEUTICAL FORM

Solution.

Cardioplegia Solution A is a sterile, non-pyrogenic solution for cardiac perfusion in a Viaflex bag. It is used to induce cardiac stasis and to protect the myocardium during open-heart surgery.

Cardioplegia Solution A is an isotonic crystalloid solution based on extracellular fluid ionic concentrations.

Approximate osmolality is 275mOsm/kg and approximate pH is 3.7.

Cardioplegia Solution A requires the aseptic addition of 10mL Sodium Bicarbonate 8.4% w/v Injection B.P. prior to use to adjust the pH to 7.4 - 7.8. Following pH adjustment the total sodium ionic concentration is 120mmol/L.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Following pH adjustment with 10mL of Sodium Bicarbonate 8.4% w/v Injection B.P., **Cardioplegia Solution A** is used in combination with ischaemia and hypothermia to induce cardiac arrest during open heart surgery and to preserve the myocardium during asystole.

4.2 Dose and method of administration

It is important that an appropriate dose of **Cardioplegia Solution A** is used to ensure that all areas of the myocardium are cooled evenly, especially those areas distal to arterial obstruction in patients with coronary-artery disease. Inadequate dosage may result in uneven cooling, incomplete arrest and ischaemic injury.

Dosage may vary depending upon the perfusion technique in use, and the preferences and experience of the surgeon. The volume of solution instilled into the aortic root may vary depending

upon the duration or type of open heart surgical procedure. The following information is provided for guidance.

The pH must be adjusted with 10mL of Sodium Bicarbonate 8.4% w/v Injection B.P. and the solution cooled to 4°C before use. Following institution of cardiopulmonary bypass at perfusate temperature of 28° to 30°C, and after cross-clamping of the ascending aorta, the pH adjusted solution is administered by rapid infusion into the aortic root. The initial rate of infusion may be 300mL/m^2/minute (approximately 540mL/min for 173cm, 70kg adult with a body surface area of 1.8m^2) given over a period of two to four minutes.

Concurrent external cooling (regional hypothermia of the pericardium) may be accomplished by instilling a refrigerated physiological solution such as **PLASMALYTE 148** (approx. pH 7.4), **Compound Sodium Lactate Infusion B.P.** (Hartmann's Solution), or a physiological ice slush into the chest cavity.

Should myocardial activity persist or recur, **Cardioplegia Solution A** may be reinfused at a rate of 300mL/m^2/minute for a period of two minutes. Reinfusion of the solution may be repeated every 20 to 30 minutes or sooner if the myocardial temperature rises above 15° to 20°C or returning cardiac activity is observed. The regional hypothermia solution around the heart may also be replenished continuously or periodically in order to maintain adequate hypothermia. Suction may be used to remove warmed infusates.

4.3 Contraindications

Cardioplegia Solution A must not be administered without the prior addition of sodium bicarbonate.

Cardioplegia Solution A must not be administered to patients with hypersensitivity to the active substance(s) or to any of the excipient listed in section 6.1.

4.4 Special warnings and precautions for use

Cardioplegia Solution A is intended only for cardiac perfusion when the coronary circulation is isolated from the systemic circulation. It must not be injected intravenously.

It should be used only by those trained in cardiac perfusion techniques and open heart surgery and in the presence of inotropic support drugs and the appropriate defibrillation equipment.

The pH of the solution must be adjusted by the aseptic addition of Sodium Bicarbonate Injection. The **Cardioplegia Solution A** container should then be rapidly inverted five times to ensure complete mixing. It should be cooled to 4°C before use. Once mixed, the solution should be used within 24 hours. It should not be used in serial connections with other containers. The remainder of any partly-used solutions should be discarded.

If large volumes of **Cardioplegia Solution A** are perfused and permitted to return to the extracorporeal circuit without any venting from the right heart, serum magnesium and potassium levels may rise. It is recommended that the right heart be vented.

It is important that the appropriate dosage of **Cardioplegia Solution A** be used (see Section 4.2) to ensure that all areas of the myocardium are cooled evenly, especially those areas distal to arterial obstruction in patients with coronary-artery disease. Inadequate dosage may result in uneven cooling, incomplete arrest and ischaemic injury.

Numerous clinical parameters require close monitoring in patients receiving **Cardioplegia Solution A**. Maintenance of hypothermia is critical and myocardial temperature should be monitored throughout the procedure. Continuous monitoring of myocardial activity is essential.

4.5 Interaction with other medicines and other forms of interaction

None stated.

4.6 Fertility, pregnancy and lactation

Pregnancy (Category B2)

Cardioplegia Solution A has not been subjected to animal reproduction studies. Its effect upon the human foetus has not been established nor has its effect upon reproductive capacity. It should be administered to pregnant women only if unavoidable.

Breast-feeding

Use of **Cardioplegia Solution A** in lactation is not recommended.

Carcinogenicity, genotoxicity, effects on fertility

Carcinogenic potential: **Cardioplegia Solution A** is based on human extracellular fluid. There is no evidence that a carcinogenic potential exists.

Genotoxicity: **Cardioplegia Solution A** is based on human extracellular fluid. There is no evidence that a mutagenic potential exists.

4.7 Effects on ability to drive and use machines

There is no information of the effects of **Cardioplegia Solution A** on the ability to drive or operate machinery.

4.8 Undesirable effects

The use of Cardioplegia solutions during open-heart surgery has been associated with a number of intraoperative and perioperative risks, including myocardial infarction, ECG abnormalities and arrhythmias (including ventricular fibrillation). Spontaneous recovery after Cardioplegia-induced cardiac arrest may be delayed or absent at reperfusion; shock defibrillation may be required to restore normal cardiac function. In addition, Cardioplegia solutions may cause potential electrolyte and acid-base abnormalities.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting/}

4.9 Overdose

Overuse of the solution may result in unnecessary dilation of the myocardial vasculature and leakage into the perivascular myocardium, possibly causing tissue oedema, see Sections 4.4 and 4.8.

For advice on the management of overdose please contact the National Poisons Centre on phone number: 0800 764 766 [0800 POISON] in New Zealand (or 131126 in Australia).

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group

Cardioplegia solutions.

ATC code

B05XA16.

Perfusion of the coronary circulation by **Cardioplegia Solution A** allows a quiet, bloodless operative field, a flaccid myocardium and avoidance of air embolism. It protects the myocardium during cardiac surgery by inducing a rapid and complete diastolic arrest, minimising myocardial energy requirements during arrest, preventing ischaemic damage during the arrest phase and minimising or preventing reperfusion injury once coronary blood flow is restored.

Sodium and Chloride
These ions have no specific role in producing cardiac arrest but are important in establishing a solution similar to the composition of normal extracellular fluid and sodium is essential in maintaining the ionic integrity of the myocardium and controlling calcium movements.

Potassium
Potassium is present in **Cardioplegia Solution A** to induce a rapid diastolic arrest, thereby preserving energy supplies (adenosine triphosphate and creatine phosphate for post-ischaemic activity.

Magnesium
Addition of magnesium to the solution prevents cellular potassium and magnesium loss, thereby conserving magnesium for its role as an enzymatic cofactor. It appears to counteract the actions of calcium in excitation-contraction coupling, which results in a reduction of energy consumption. It also has a weak arresting action on the heart.

Calcium
Calcium helps maintain the integrity of the cell membrane and prevents a condition known as "calcium paradox" occurring during reperfusion.

Bicarbonate
This is added to adjust the pH, producing a slightly alkaline (7.4 - 7.8) solution and to compensate for the metabolic acidosis which accompanies ischaemia.

5.2 Pharmacokinetic properties
None stated.

5.3 Preclinical safety data
Cardioplegia Solution A has not been subjected to animal reproduction studies.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Water for injection.

6.2 Incompatibilities
Additives may be incompatible.

6.3 Shelf life
24 months.

6.4 Special precautions for storage
Store at or below 30°C.

6.5 Nature and contents of container
Cardioplegia Solution A is supplied in 1000mL Viaflex plastic containers for single use only.

6.6 Special precautions for disposal and other handling.

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

The pH of the solution must be adjusted to between 7.4 and 7.8 with 10mL Sodium Bicarbonate 8.4% w/v Injection BP (not supplied) before use.

7 MEDICINE SCHEDULE

General Sale Medicine.

8 SPONSOR

Cardioplegia Solution A *is distributed in New Zealand by:*

Baxter Healthcare Ltd
33 Vestey Drive
Mt Wellington
Auckland 1060.

Baxter Healthcare Ltd
PO Box 14 062
Panmure
Auckland 1741

Phone (09) 574 2400.

Cardioplegia Solution A *is manufactured and distributed in Australia by:*

Baxter Healthcare Pty Ltd
1 Baxter Drive
Old Toongabbie, NSW 2146.

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine: 7 April 2016.

10 DATE OF REVISION OF THE TEXT

23 May 2018.

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
All	Entire document reformatted to new standard format based on the European Summary of Product Characteristics (SPC).

Based on Australian PI most recent amendment 24 February 2015; and CCSI43220140228.

Please refer to the Medsafe website (www.medsafe.govt.nz) for most recent data sheet.