1.3.1 Summary of Product Characteristics:

1. Name of the medicinal product

Cardesine 6mg/2ml Solution for intravenous injection.

2. Qualitative and quantitative composition

Vial contains 6 mg of Adenosine as active substance.

3. Pharmaceutical form

Solution for intravenous injection.

4. Clinical particulars

4.1 Therapeutic indications

CARDESINE® contains a medicine called adenosine. This belongs to a group of medicines called antiarrhythmic.

CARDESINE® works by slowing down electrical impulses between the upper and lower chambers of the heart. This slows the fast or uneven heartbeats called arrhythmias.

CARDESINE® is used:

- During a test. This is to help doctors find out what type of arrhythmia (uneven heart beat) you have.
- To bring your heart beat back to normal if you have a type of arrhythmia called 'paroxysmal supraventricular tachycardia (SVT)' or 'Wolff- Parkinson-White Syndrome'.

4.2 Posology and method of administration

CARDESINE® is intended for hospital use only with monitoring and cardiorespiratory resuscitation equipment available for immediate use. It should be administered by rapid IV bolus injection according to the ascending dosage schedule below. To be certain the solution reaches the systemic circulation administer either directly into a vein or into an IV line. If given into an IV line it should be injected as proximally as possible, and followed by a rapid saline flush.

CARDESINE® should only be used when facilities exist for cardiac monitoring. Patients who develop high-level AV block at a particular dose should not be given further dosage increments.

Therapeutic dose:

Adult

- Initial dose: 3 mg given as a rapid intravenous bolus (over 2 seconds).
- Second dose: if the first dose does not result in elimination of the supraventricular tachycardia within 1to 2 minutes, 6mg should be given also as a rapid intravenous bolus.
- Third dose: if the second dose does not result in elimination of the supraventricular tachycardia within 1 to 2 minutes, 12 mg should be given also as a rapid intravenous bolus.

Additional or higher doses are not recommended.

Children

No controlled pediatric study has been undertaken. Published uncontrolled studies show similar effects of adenosine in adults and children: effective doses for children were between 0.0375 and 0.25 mg/kg.

Elderly
See dosage recommendations for adults.
Diagnostic dose:
The above ascending dosage schedule should be employed until sufficient diagnostic information has been obtained.
Method of administration: Rapid intravenous injection only.
How CARDESINE® is given
- **CARDESINE®** is a medicine for use in hospitals.
- It will be given to you by a doctor or nurse as an injection into your vein.
- Your heart and blood pressure will be closely monitored.

How much CARDESINE® is given?
If you are not sure why you are being given **CARDESINE®** or have any questions about how much **CARDESINE®** is being given to you; speak to your doctor, nurse or pharmacist.
Adults (including the elderly):
- The first dose is 3 mg given over 2 seconds. This is given by rapid injection into your vein.
- If the first dose does not bring your heart beat to normal then you will be given a second dose. The second dose is 6 mg given as a rapid injection.
- If the second dose does not bring your heart beat to normal then you will be given a third dose. The third dose is 12mg given as a rapid injection.
- You should not have any more doses after the 12 mg dose.

Children:
The hospital specialist will decide if this medicine is needed and how much should be given.

4.3 Contraindications

Do not have this medicine and tell your doctor if:
- You are allergic (hypersensitive) to adenosine or any of the other ingredients of **CARDESINE®**.

Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue.
- You have asthma or any other severe breathing problem;
- You have very low blood pressure (severe hypotension);
- You have a type of heart failure where your heart is not pumping out enough blood;
- You have problems with your heart rhythm and do not have a pace maker (second or third degree Atrio entricular block, sick sinus syndrome);
- You have been told you have 'Long QT syndrome'. This is a rare heart problem that can lead to a fast heart beat and fainting.

Do not have this medicine if any of the above applies to you. If you are not sure, talk to your doctor, nurse or pharmacist before you are given **CARDESINE®**.

4.4 Special warnings and precautions for use

Check with your doctor, nurse or pharmacist before you have **CARDESINE®** if:

- You have a certain type of unusual heart rhythm (atrial fibrillation or atrial flutter) and in particular if you have an 'accessory conduction pathway';
- You have been told that you have a heart problem whereby the electrical impulses in parts of your heart take longer than normal to discharge and then, recharge (prolonged QT interval);
- You have low blood volume (hypovolemia) that is no adequately corrected by treatment with medicines;
- You have problems with a part of your nervous system called the 'autonomic nervous system';
- You have narrowing of the main arteries in the neck (carotid artery). This means that not enough blood is getting to the brain (cerebrovascular insufficiency);
- You have or have ever had fits or convulsions;
- You have difficulty in breathing (bronchospasm);
- You have heart disease due to narrowing of your heart valves (stenotic valvular heart disease);
- You have inflammation of the membrane surrounding your heart (pericarditis) or a build-up of fluid around your heart (pericardial effusion);
- You have a left-right shunt in your heart. This will mean blood goes directly from the left side of your heart to the right side;
- You have narrowing of the left main artery supplying blood to your heart (left main coronary stenosis);
- You have had a recent heart attack, severe heart failure or you have had a heart transplant in the last year;
- You have any minor problem with your heart (first degree AtrioVentricular block or bundle branch block).

These conditions maybe temporarily aggravated when you are given **CARDESINE®**.

If you get a very slow heartbeat (severe bradycardia), respiratory failure, a heart problem that can be fatal (asystole), severe chest pains (angina) or very low blood pressure (severe hypotension), then treatment with **CARDESINE®** should be stopped. If you are not sure if any of the above applies to you, talk to your doctor or nurse before being given **CARDESINE®**.

Important information about some of the ingredients of CARDESINE®:

Sodium: **CARDESINE®** injection contains 3.54 mg sodium per dose (7.08 mg/2 ml vial). This should be taken into consideration by patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Please tell your doctor, nurse or pharmacist if you are taking or have recently taken any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because **CARDESINE®** can affect the way some other medicines work. Also some medicines can affect the way **CARDESINE®** works.

In particular, check with your doctor, nurse or pharmacist if you are taking any of the following:

- Dipyridamole (medicine used to thin the blood), make sure your doctor knows you are taking dipyridamole. Your doctor may decide you should not have **CARDESINE®** or may need to give you a lower dose of **CARDESINE®**.

- Aminophylline or theophylline (medicines used to help breathing),
- Caffeine (sometimes found in headache in medicines).

Taking CARDESINE® with food and drink:

Food and **CARDESINE®** containing caffeine such as tea, coffee, chocolate and cola should be avoided for at least 12 hours before you are given **CARDESINE®**.

4.6 pregnancy and lactation

Talk to your doctor or nurse before having this medicine if:

- You are pregnant, might become pregnant, or think that you may be pregnant. You should not be given **CARDESINE®** if you are pregnant or think you may be pregnant, unless clearly necessary;
- You are breast-feeding. You should not be given **CARDESINE®** if you are breast-feeding.

Ask your doctor or nurse for advice before taking any medicine if you are pregnant or breast-feeding.

4.7 Effects on ability to drive and use machines

Not Applicable.

4.8 Undesirable effects

Like all medicines, **CARDESINE®** can cause side effects, although not everybody gets them. While you are being given **CARDESINE®** you may have some of the following side effects:

If any of the following side effects get worse, tell your doctor or nurse and they may stop the injection:

The side effects normally settle within seconds or minutes after the injection is finished but you should tell your doctor or nurse if any of them happen.

Very common (affects more than 1 person in 10)

- Reddening of skin with a feeling of heat (flushing),
- Slow heartbeat (bradycardia),
- Skipped heart beats or extra heartbeats,
- A heart problem called an AV block,
- Severe heart problems which can be fatal (asystole) or uneven heartbeat,
- Shortness of breath or the urge to breathe deeply (dyspnea),
- Chest pain or pressure on the chest.
- Feeling dizzy or light-headed,
- Feeling sick (nausea),
- Headache,
- Unusual skin sensations such as burning,
- Feeling nervous.
- Blurred vision,
- Being aware of your heartbeat or feeling it 'racing',
- Metallic taste in your mouth,
- Breathing more quickly or more deeply than normal (hyperventilation),
- Feeling pressure in your head, or weighed down in your arms,
- Feeling of general discomfort, weakness or pain,
- Sweating.

- Severe breathlessness or problems in breathing,
- Redness, pain or swelling at the site of injection,
- Feeling uncomfortable during the injection,
- Worsening of high blood pressure that affects the brain (intracranial hypertension),
- Very slow, fast or uneven heartbeats,
- Severe bradycardia (very slow heartbeat).
- Fainting,
- Fits (convulsions),
- Being sick (vomiting),
- Stopping breathing (respiratory arrest).

If any of the above side effects get worse, tell your doctor or nurse and they may stop the injection. The side effects normally settle within seconds or minutes after the injection is finished but you should tell your doctor or nurse if any of them happen.
If you notice any side effects not listed in this leaflet, please tell your doctor or nurse.

4.9 Overdose

As this medicine is given to you by a doctor or nurse it is unlikely that you will be given too much. Your doctor will carefully work out how much **CARDESINE®** you should be given.
As the length of time adenosine stays in the blood is very short, any side effects of too much **CARDESINE®** would quickly stop when the injection is stopped. Sometimes you may need an injection of a medicine called aminophylline or theophylline to help with any side effects.
If you have any further questions on the use of this medicine, ask your doctor, nurse or pharmacist.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:	• Antiarrhythmic Agent, Miscellaneous • Diagnostic Agent
ATC code:	C01EB10

Antiarrhythmic actions: Slows conduction time through the AV node, interrupting the re-entry pathways through the AV node, restoring normal sinus rhythm

Myocardial perfusion scintigraphy: Adenosine also causes coronary vasodilation and increases blood flow in normal coronary arteries with little to no increase in stenotic coronary arteries; thallium -201 uptake into the stenotic coronary arteries will be less than that of normal coronary arteries revealing areas of insufficient blood flow.

Hemodynamic Effects: Adenosine produces a direct negative chronotropic, dromotropic and inotropic effect on the heart, presumably due to A1-receptor agonism, and produces peripheral vasodilation, presumably due to A2-receptor agonism. The net effect of Adenosine injection in humans is typically a mild to moderate reduction in systolic, diastolic and mean arterial blood pressure associated with a reflex increase in heart rate. Rarely, significant hypotension and tachycardia have been observed

5.2 Pharmacokinetic properties

Distribution

Intravenously administered Adenosine distributes from the circulation via cellular uptake, primarily by erythrocytes and vascular endothelial cells. This process involves a specific transmembrane nucleoside carrier system that is reversible, nonconcentrative, and bidirectionally symmetrical.

Metabolism

Intracellular Adenosine is metabolized either via phosphorylation to Adenosine monophosphate by Adenosine kinase, or via deamination to inosine by Adenosine deaminase in the cytosol. Since Adenosine kinase has a lower Km and Vmax than Adenosine deaminase, deamination plays a significant role only when cytosolic Adenosine saturates the phosphorylation pathway. Inosine formed by deamination of Adenosine can leave the cell intact or can be degraded to hypoxanthine, xanthine, and ultimately uric acid. Adenosine monophosphate formed by phosphorylation of Adenosine is incorporated into the high-energy phosphate pool.

Elimination

While extracellular Adenosine is primarily cleared from plasma by cellular uptake with a half-life of less than
10 seconds in whole blood, excessive amounts may be deaminated by an ecto-form of Adenosine deaminase.

5.3 Preclinical safety data

Not Applicable.

6. Pharmaceutical particulars

6.1 List of excipients

Sodium Chloride, Hydrochloric Acid and Water for injection.

6.2 Incompatibilities

Not Applicable.

6.3 Shelf life

2 years

6.4 Special precautions for storage
Do not store above 30°C, do not refrigerate.

6.5 Nature and contents of container
VIAL3ml and Rubber Stopper 13mm

6.6 Special precautions for disposal and other handling
Not Applicable.

1.7 Marketing Authorisation Holder
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Amman/ Jordan /Sahab- street no.6, building no.356
Tel: 06-4020680
Fax: 06-4020681
06-4162905
MS Pharma Jordan is responsible for the manufacture, packaging and QC Testing of this product& batch releasing to the market.