DATA SHEET

1 ADENOCOR 6 MG/2 ML SOLUTION FOR INTRAVENOUS INFUSION

ADENOCOR 6 mg/2 mL solution for intravenous infusion.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 6 mg of adenosine per 2 mL.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for intravenous infusion

Clear, colourless solution

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Therapeutic Indications

Rapid conversion to a normal sinus rhythm of paroxysmal supraventricular tachycardias, including those associated with accessory bypass tracts (Wolff-Parkinson-White syndrome).

Diagnostic Indications

Aid to diagnosis of broad or narrow QRS complex supraventricular tachycardias. Although ADENOCOR is not effective in converting atrial flutter, atrial fibrillation or ventricular tachycardia to sinus rhythm, the slowing of AV conduction helps diagnosis of atrial activity.

Sensitisation of intracavity electrophysiological investigations.

4.2 DOSE AND METHOD OF ADMINISTRATION

Method of Administration

ADENOCOR should be used only in hospitals, with monitoring and cardiorespiratory resuscitation equipment available for immediate use if necessary. 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, it should be administered either directly into a vein or into an IV line. If administered via an IV line it should be injected as proximally as possible, and followed by a rapid saline flush.

ADENOCOR 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

Adults

Initial dose: 3 mg given as a rapid intravenous bolus (over 2 seconds).

Second dose: If the first dose does not result in the elimination of supraventricular tachycardia within 1 or 2 minutes, 6 mg should be given also as a rapid intravenous bolus.

Third dose: If the second dose does not result in the elimination of supraventricular tachycardia within 1 or 2 minutes, 12 mg should be given also as a rapid intravenous bolus.

Paediatric population

No controlled paediatric studies have been undertaken. The level of evidence does not allow a recommended posology.

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.

4.3 CONTRAINDICATIONS

ADENOCOR is contraindicated in patients with:

- known hypersensitivity to adenosine or to any of the excipients in section 6.1.
- sick sinus syndrome, second or third degree AV block (except in patients with a functioning artificial pacemaker)
- chronic obstructive lung disease (such as asthma)
- long QT syndrome
- severe hypotension
- decompensated states of heart failure.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Adenosine is intended for use by physicians familiar with the product (see section 4.2) in a hospital setting with monitoring and cardio-respiratory resuscitation equipment available for immediate use if necessary.

The occurrence of angina, severe bradycardia, severe hypotension, respiratory failure (potentially fatal), or asystole/cardiac arrest (potentially fatal), should lead to immediate discontinuation of administration.

In patients with history of convulsions/seizures, the administration of adenosine should be carefully monitored.

As dipyridamole is a known inhibitor of adenosine uptake, it may potentiate the action of adenosine administration. The use of Adenoscan infusion is contraindicated in patients receiving dipyridamole (see Adenoscan Product Information: 'CONTRAINDICATIONS'). If use of adenosine bolus injection (ADENOCOR) is judged to be essential, dipyridamole should be discontinued 24 hours beforehand or the dose of adenosine should be significantly reduced.

ADENOCOR (adenosine) should be given as a rapid intravenous bolus. Adenosine is ineffective in the management of SVT when given as an infusion, rather than a bolus. This is most probably due to the different effect on sinus rate and atrioventricular nodal conduction.

Hypotension

Because it has the potential to cause significant hypotension, adenosine should be used with caution in patients with left main coronary stenosis, uncorrected hypovolaemia, stenotic valvular heart disease, left to right shunt, pericarditis or pericardial effusion, autonomic dysfunction or stenotic carotid artery disease with cerebrovascular insufficiency.

Atrial Fibrillation

ADENOCOR should be used with caution in patients with atrial fibrillation or flutter and especially in those with an accessory by-pass tract since particularly the latter may develop increased conduction down the anomalous pathway.

Bradycardia

Some cases of severe bradycardia have been reported. Some occurred in early post heart transplant patients; in other cases occult sino-atrial disease was present. The occurrence of severe bradycardia should be taken as a warning of underlying disease and could potentially favour the occurrence of torsades de pointes.

Heart Block and Myocardial Infarction

ADENOCOR (adenosine) exerts its effect by decreasing conduction through the AV node and may produce a short lasting first, second or third-degree heart block. In extreme cases, transient asystole may result (one case has been reported in a patient with atrial flutter who was receiving carbamazepine). Appropriate therapy should be instituted as needed. Patients who develop high level block on one dose of ADENOCOR should not be given additional doses. Because of the very short half-life of adenosine, these effects are generally self-limiting.

ADENOCOR should be used with caution in patients with recent myocardial infarction, heart failure, or in patients with minor conduction defects (first degree AV block, bundle branch block) that could be transiently aggravated during infusion.

Arrhythmias at Time of Conversion

At the time of conversion to normal sinus rhythm, a variety of new rhythms may appear on the electrocardiogram. They generally last only a few seconds without intervention and may take the form of premature ventricular contractions, premature atrial contractions, atrial fibrillation, sinus bradycardia, sinus tachycardia, skipped beats, sinus pause and varying degrees of AV nodal block. Such findings were seen in 55% of patients. The induced bradycardia predisposes the patient to ventricular excitability disorders including ventricular fibrillation and torsades de pointes.

Because of the possible risk of torsades de pointes, ADENOCOR should be used with caution in patients with a prolonged QT interval.

Post Heart Transplantation

In patients with recent heart transplantation (less than 1 year) an increased sensitivity of the heart to adenosine has been observed. ADENOCOR should be used with caution in such cases.

Bronchoconstriction

Adenosine administered by inhalation has been reported to cause bronchoconstriction in asthmatic patients, presumably due to mast cell degranulation and histamine release. These effects have not been observed in normal subjects. Adenosine has been administered to a limited number of patients with asthma and mild to moderate exacerbation of their symptoms has been reported. ADENOCOR should not be used in patients with asthma (see section 4.3).

Respiratory compromise has occurred during adenosine infusion in patients with obstructive pulmonary disease. ADENOCOR should be used with caution in patients with obstructive lung disease not associated with bronchoconstriction (e.g. emphysema, bronchitis, etc.) and should be avoided in patients with bronchoconstriction or bronchospasm (e.g. asthma). ADENOCOR should be discontinued in any patient who develops severe respiratory difficulties.

Adenosine may precipitate or aggravate bronchospasm.

Paediatric Use

ADENOCOR may trigger atrial arrhythmias and thus might lead to ventricular acceleration in children with Wolff-Parkinson-White (WPW) syndrome. Also see section 5.1.

The efficacy of intraosseous administration has not been established.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

Intravenous ADENOCOR (adenosine) has been effectively administered in the presence of other cardioactive drugs, such as digitalis, quinidine, beta-adrenergic blocking agents, calcium-channel blocking agents, and angiotensin-converting enzyme inhibitors, without any change in the adverse reaction profile.

Adenosine may interact with drugs that tend to impair cardiac conduction.

Aminophylline, theophylline and other xanthines are competitive adenosine antagonists and should be avoided for 24 hours prior to the administration of adenosine.

Food and drinks containing xanthines (e.g. tea, coffee, chocolate and cola) should be avoided for at least 12 hours prior to the administration of adenosine.

Nucleoside transport inhibitors such as dipyridamole inhibit adenosine cellular uptake and metabolism, and potentiate the action of adenosine. In one study dipyridamole was shown to produce a four-fold increase in adenosine activity. The use of Adenoscan infusion is contraindicated in patients receiving dipyridamole (see Adenoscan Product Information: ‘CONTRAINDICATION’). If the use of adenosine bolus injection (ADENOCOR) is judged to be essential, dipyridamole should be discontinued 24 hours beforehand, or the dose of ADENOCOR should be significantly reduced.

Carbamazepine has been reported to increase the degree of heart block produced by other agents. As the primary effect of adenosine is to decrease conduction through the AV node, higher degrees of heart block may be produced in the presence of carbamazepine.

4.6 FERTILITY, PREGNANCY AND LACTATION

Use in Pregnancy

Category B2

Animal reproductive studies have not been conducted with adenosine, nor have studies been performed on pregnant women. In the absence of evidence that adenosine does not cause foetal harm, ADENOCOR should not be used during pregnancy unless the physician considers the benefits outweigh the potential risks.

Use in Lactation

Studies have not been performed in lactating animals or women. Therefore, adenosine should not be used during lactation. If adenosine treatment is considered essential by the physician, another form of infant feeding should be considered.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not applicable.

4.8 UNDESIRABLE EFFECTS

The following adverse reactions have been reported with adenosine rapid intravenous bolus injection. These adverse reactions have been classified using standard terminology and are categorised by body system. They are listed in order of decreasing frequency according to the following definitions:

very common:	≥ 1/10 (10%)
common:	≥ 1/100 (1%) and < 1/10 (10%)
uncommon:	≥ 1/1000 (0.1%) and < 1/100 (1%)
rare:	≥ 1/10000 (0.01%) and < 1/1000 (0.1%)
very rare:	< 1/10000 (0.01%)
not known:	(cannot be estimated from available data)

Cardiovascular System

Very common: bradycardia; sinus pause, skipped beats; atrial extrasystoles; A-V block; ventricular excitability disorders such as ventricular extrasystoles, non-sustained ventricular tachycardia.

Uncommon: sinus tachycardia; palpitations.

Very rare: atrial fibrillation; ventricular excitability including ventricular fibrillation and torsade de pointes; severe bradycardia not corrected by atropine and possibly requiring temporary pacing.

Not known: asystole/cardiac arrest, sometimes fatal especially in patients with underlying ischemic heart disease/cardiac disorder; MI/ST segment elevation especially in patients with pre-existing severe CAD; cerebrovascular accident/transient ischemic attack, secondary to the hemodynamic effects of adenosine including hypotension; arteriospasm coronary which may lead to myocardial infarction; hypotension sometimes severe.

Respiratory System

Very common: dyspnoea (or the urge to breathe deeply).

Uncommon: hyperventilation.

Very rare: bronchospasm.

Not known*:* respiratory failure; apnoea/respiratory arrest.

Central Nervous System

Common: headache; dizziness, light-headedness.

Uncommon: head pressure.

Very rare: transient and spontaneously rapidly reversible worsening of intracranial hypertension.

Not known*:* loss of consciousness/syncope; convulsions, especially in predisposed patients.

Gastrointestinal System

Common: nausea.

Uncommon: metallic taste.

Not known*:* Vomiting.

Other

Very common: flushing; chest pressure/pain, feeling of thoracic constriction/oppression.

Common: apprehension; burning sensation.

Uncommon: blurred vision; sweating; feeling of general discomfort/weakness/pain.

Very rare: injection site reactions.

Not known*:* anaphylactic reaction (including angioedema and skin reactions such as urticaria and rash).

Postmarketing Experience

In postmarket clinical experience with ADENOCOR, hypotension, sometimes severe, has been reported. There have been reports of cerebrovascular accident/transient ischemic attack, secondary to the hemodynamic effects of adenosine, including hypotension.

Cases of asystole/cardiac arrest, sometimes fatal especially in patients with underlying ischaemic heart disease/cardiac disorder have been reported (see section 4.4).

Loss of consciousness/syncope, and convulsions especially in predisposed patients have been reported (see section 4.4).

Apnoea/respiratory arrest, and respiratory failure (see section 4.4) have been reported. Cases of fatal outcome of respiratory failure, of bronchospasm, and of apnoea/respiratory arrest have also been reported.

Cases of vomiting have been reported.

Other reports include tingling in arms, numbness, pressure in groin and transient increase in blood pressure.

Myocardial infarction and ST segment elevation have been reported, especially in patients with pre-existing severe coronary artery disease.

Anaphylactic reactions, including angioedema and skin reactions such as urticaria and rash, have been reported.

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

As the half-life of adenosine is very short (less than 10 seconds), adverse effects are generally rapidly self-limiting. Treatment of any prolonged adverse effects should be individualised and be directed toward the specific symptoms. Methylxanthines, such as caffeine and theophylline, and aminophylline are competitive antagonists of adenosine. Intravenous aminophylline or theophylline may be needed.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

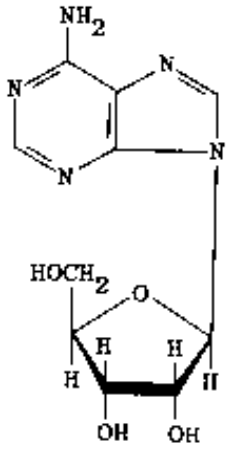
5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Pharmacotherapeutic group: Other Cardiac Preparations, ATC code: C01EB10

Description

Adenosine is designated chemically as 6-amino-9-ß-D-ribofuranosyl-9-H-purine and has the following chemical structure:



Adenosine is a white crystalline powder slightly soluble in water with a molecular weight of 267.2 and an empirical formula of $C_{10}H_{13}N_5O_4$.

ADENOCOR is a sterile solution for intravenous injection (rapid bolus), provided in clear glass vials. Each vial contains 6 mg of adenosine in 2 mL of a 0.9% w/v solution of sodium chloride in sterile water for injections.

Mechanism of Action

ADENOCOR administered by rapid intravenous injections depresses conduction through the AV node. This action can interrupt re-entry circuits involving the AV node and restore normal sinus rhythm in patients with paroxysmal supraventricular tachycardias and paroxysmal supraventricular tachycardias associated with Wolff-Parkinson-White Syndrome. Once the circuit has been interrupted, the tachycardia stops and normal sinus rhythm is re-established.

By transiently slowing AV conduction, atrial activity is easier to evaluate from ECG recordings and therefore ADENOCOR can aid the diagnosis of broad or narrow QRS complex tachycardias.

ADENOCOR may be useful during electrophysiological studies to determine the site of AV block or to determine, in some cases of pre-excitation, whether conduction is occurring by an accessory pathway or via the AV node.

Haemodynamics

The usual intravenous bolus dose of 3 or 6 mg ADENOCOR usually has no systemic haemodynamic effects. Rarely significant hypotension and tachycardia have been observed. When larger doses are given by infusion, adenosine decreases blood pressure by decreasing peripheral resistance.

5.2 PHARMACOKINETIC PROPERTIES

Intravenously administered ADENOCOR (adenosine) is removed from the circulation very rapidly. Following an intravenous bolus, adenosine is taken up by erythrocytes and vascular endothelial cells. The half-life of intravenous adenosine is estimated to be less than 10 seconds. Adenosine enters the body pool and is primarily metabolised to inosine and adenosine monophosphate (AMP).

Hepatic and Renal Failure

Hepatic and renal failure should have no effect on the activity of a bolus ADENOCOR (adenosine) injection. Since ADENOCOR (adenosine) has a direct action, hepatic and renal function are not required for the activity or metabolism of a bolus adenosine injection.

5.3 PRECLINICAL SAFETY DATA

Carcinogenicity / Mutagenicity

Studies in animals have not been performed to evaluate the carcinogenic potential of ADENOCOR. Adenosine tested negative for mutation in the Salmonella/Mammalian Microsome Assay. Adenosine, like other nucleosides at millimolar concentrations present for several doubling times of cells in culture, is known to produce a variety of chromosomal alterations. In

rats and mice, adenosine administered intraperitoneally once a day for 5 days at 50, 100 and 150 mg/kg caused decreased spermatogenesis and increased numbers of abnormal sperm.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Sodium chloride

Water for injections

6.2 INCOMPATIBILITIES

In the absence of compatibility studies, this medicine must not be mixed with other medicines.

6.3 SHELF LIFE

3 years

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25°C. Do not refrigerate.

Any portion of the vial not used at once should be discarded.

6.5 NATURE AND CONTENTS OF CONTAINER

Clear, type I glass vials with chlorobutyl rubber closures secured with aluminium caps. Packs of 6 vials in plastic trays in cardboard cartons.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

No special requirements for disposal.

7 MEDICINE SCHEDULE

Prescription Medicine

8 SPONSOR

Pharmacy Retailing (NZ) Ltd t/a Healthcare Logistics
PO Box 62027
Sylvia Park Auckland 1644
Freecall: 0800 283 684
Email: medinfo.australia@sanofi.com

9 DATE OF FIRST APPROVAL

15 December 1994

10 DATE OF REVISION OF THE TEXT

02 September 2022

Table 1 - Summary of Changes

Section	Change
4.8	Addition of undesirable effects with frequency 'not known' Addition of arteriospasm coronary