

# PRODUCT INFORMATION

# ADENOSINE MYLAN

# INJECTION

Adenosine 6mg/2mL

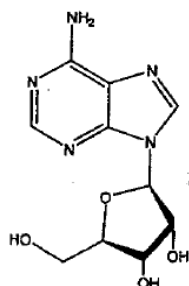


## NAME OF THE MEDICINE

Active ingredient : Adenosine

Chemical name : 9-β-D-ribofuranosyl-9H-purin-6-amine

Structural formula :



Molecular formula : C<sub>10</sub>H<sub>13</sub>N<sub>5</sub>O<sub>4</sub>

Molecular weight : 267.2

CAS Registry no. : 58-61-7

## DESCRIPTION

Adenosine is a white, crystalline powder slightly soluble in water, soluble in hot water, practically insoluble in alcohol and in methylene chloride.

Adenosine Mylan is a sterile solution for intravenous injection (rapid bolus), available in clear glass vials and pre-filled syringes. Each vial or pre-syringe contains adenosine and sodium chloride in water for injections, pH between 4.5 and 7.5.

## PHARMACOLOGY

Adenosine administered by rapid intravenous injection depresses conduction through the atrioventricular (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 adenosine can aid the diagnosis of broad or narrow QRS complex tachycardias.

Adenosine 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 intravenous bolus dose of 3 mg or 6 mg adenosine 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.

## Pharmacokinetics

Intravenously administered 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 or Renal Failure:** Hepatic and renal failure should have no effect on the activity of a bolus injection of adenosine. Since adenosine has a direct action, hepatic and renal functions are not required for the activity or metabolism of a bolus injection.

## INDICATIONS

### Therapeutic Indications

Adenosine Mylan is indicated for the rapid conversion to a normal sinus rhythm of paroxysmal supraventricular tachycardias, including those associated with accessory bypass tracts (Wolff-Parkinson-White syndrome).

### Diagnostic Indications

Adenosine Mylan is indicated as an aid to diagnosis of broad or narrow QRS complex supraventricular tachycardias. Although adenosine 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. In this respect adenosine should be used as an adjunct to, but not a replacement for, clinical and ECG observations. It should be used only when, despite all diagnostic attempts, doubt still persists.

Adenosine Mylan can also be used for improved diagnostic sensitivity of intracavity electrophysiological investigations.

## CONTRAINDICATIONS

Adenosine Mylan is contraindicated in patients suffering from:

- known hypersensitivity to adenosine
- 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

## PRECAUTIONS

Adenosine is intended for use by doctors familiar with the product (see **DOSAGE AND ADMINISTRATION**) in a hospital setting with monitoring and cardiorespiratory 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 a 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. If the use of adenosine bolus injection (Adenosine Mylan) is judged to be essential, dipyridamole should be discontinued 24 hours beforehand, or the dose of adenosine should be significantly reduced.

Adenosine should be given as a rapid intravenous bolus injection. Adenosine is ineffective in the management of supraventricular tachycardias 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**

Adenosine should be used with caution in patients with atrial fibrillation or flutter and especially in those with an accessory bypass 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 sinoatrial 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**

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 adenosine should not be given additional doses. Because of the very short half-life of adenosine, these effects are generally self-limiting.

Adenosine should be used with caution in patients with recent myocardial infarction, heart failure or in patients with minor conduction defects (first degree A-V 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 torsade de pointes.

Because of the possible risk of torsade de pointes, adenosine 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. Adenosine 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. Adenosine should not be used in patients with asthma (See **CONTRAINDICATIONS**).

Respiratory compromise has occurred during adenosine infusion in patients with obstructive pulmonary disease. Adenosine 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). Adenosine should be discontinued in any patient who develops severe respiratory difficulties.

Adenosine may precipitate or aggravate bronchospasm.

### **Carcinogenicity, mutagenicity and effects on fertility**

Studies in animals have not been performed to evaluate the carcinogenic potential of adenosine. 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.

### **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, adenosine should not be used during pregnancy unless the doctor 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 doctor, another form of infant feeding should be considered.

### **Paediatric use**

No data has been submitted from controlled studies in children.

## **INTERACTIONS WITH OTHER MEDICINES**

Intravenous adenosine has been administered effectively 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 eg 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 fourfold increase in adenosine activity. If the use of adenosine bolus injection (Adenosine Mylan) is judged to be essential, dipyridamole should be discontinued 24 hours beforehand, or the dose of adenosine 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.

## ADVERSE EFFECTS

The following adverse reactions were 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:  $\geq 1/10$  (10%)

common:  $\geq 1/100$  (1%) and  $< 1/10$  (10%)

uncommon:  $\geq 1/1,000$  (0.1%) and  $< 1/100$  (1%)

rare:  $\geq 1/10,000$  (0.01%) and  $< 1/1,000$  (0.1%)

very rare:  $< 1/10,000$  (0.01%)

### Cardiovascular system:

Very common: Bradycardia; sinus pause, skipped beats; atrial asystoles; A-V block; ventricular excitability disorders such as ventricular asystoles, nonsustained ventricular tachycardia.

Uncommon: sinus tachycardia; palpitations.

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

### Respiratory system:

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

Uncommon: hyperventilation.

Very rare: bronchospasm.

### Central Nervous System:

Common: headache; dizziness; lightheadedness.

Uncommon: head pressure.

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

### Gastrointestinal system:

Common: nausea

Uncommon: metallic taste.

### Other:

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

Common: apprehension; burning and sensation.

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

Very rare: injection site reactions.

**Post-marketing experience:**

In post market clinical experience, hypotension, sometimes severe, has been reported. Cases of asystole / cardiac arrest, sometimes fatal, especially in patients with underlying ischaemic heart disease / cardiac disorder have been reported (see **PRECAUTIONS**).

Loss of consciousness / syncope and convulsions especially in predisposed patients have been reported (see **PRECAUTIONS**).

Apnoea / respiratory arrest and respiratory failure (see **PRECAUTIONS**) 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 the 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.

**DOSAGE AND ADMINISTRATION**

Adenosine Mylan should be used only in hospitals with monitoring and cardiorespiratory resuscitation equipment available for immediate use. It should be administered by rapid intravenous 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 administered into an IV line it should be injected as proximally as possible, and followed by a rapid saline flush.

Adenosine Mylan 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.

Adenosine Mylan is for use in one patient only. Discard any remaining contents.

**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 the 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 the supraventricular tachycardia within 1 or 2 minutes, 12 mg should be given, also as a rapid intravenous bolus.

**Children:**

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

## OVERDOSAGE

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.

Contact the Poisons Information Centre on 131126 for advice on management of overdosage.

## PRESENTATION AND STORAGE CONDITIONS

Adenosine Mylan 6 : Injection, solution  
mg/2 mL

Glass vials. Available in packs of 6 x 2 mL

Store below 30°C. Protect from light.

Adenosine Mylan 6 : Injection, solution  
mg/2 mL

Glass, Pre-filled syringes. Available in packs of 5 syringes

Store below 30°C. Protect from light.

Do not refrigerate as crystallisation may occur. If crystallisation has occurred, dissolve crystals by warming to room temperature. The solution should be clear at time of use. Any portion of the vial not used at once should be discarded.

Some strengths, pack sizes and/or pack types may not be marketed..

## NAME AND ADDRESS OF THE SPONSOR

### Alphapharm Pty Limited

Level 1, 30 The Bond

30-34 Hickson Road

Millers Point NSW 2000

ABN 93 002 359 739

[www.mylan.com.au](http://www.mylan.com.au)

## POISON SCHEDULE OF THE MEDICINE

S4 (Prescription Only Medicine)

## DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

10th August 2009

## **DATE OF MOST RECENT AMENDMENT**

17/03/2017

**Adenosine Mylan\_pi\Mar17/00**