PRODUCT MONOGRAPH

[Pr]Adenosine Injection, USP
(adenosine injection, USP, 3mg/mL)

Sterile

6 mg / 2 mL Prefilled Syringe

Antiarrhythmic

Mylan Pharmaceuticals ULC
85 Advance Road
Etobicoke, ON
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Date of Preparation: July 16, 2014

Submission Control No: 175322

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[Pr]Adenosine Injection, USP
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THERAPEUTIC CLASSIFICATION

Antiarrhythmic

PART I: HEALTH PROFESSIONAL INFORMATION

ACTION AND CLINICAL PHARMACOLOGY

Adenosine Injection is an endogenous nucleoside occurring in all cells of the body. When injected intravenously adenosine slows atrioventricular (A-V) nodal conduction, can interrupt the reentry pathways through the A-V node and can restore normal sinus rhythm in patients with paroxysmal supraventricular tachycardia (PSVT), including PSVT associated with Wolff-Parkinson-White syndrome.

Adenosine is antagonized competitively by methylxanthines such as caffeine and theophylline and potentiated by blockers of nucleoside transport such as dipyridamole. Adenosine is not blocked by atropine.

In controlled clinical trials, cumulative 60% and 92% of patients converted to normal sinus rhythm within one minute after 6 mg and 12 mg bolus doses of Adenosine Injection, respectively. In other controlled clinical trials with bolus doses of 3, 6, 9 and 12 mg some patients with paroxysmal supraventricular tachycardia converted to normal sinus rhythm on 3 mg of Adenosine Injection. Reports in the medical literature indicate success in treating PSVT in pediatric patients (including newborns) with Adenosine Injection in doses equivalent by weight to those used in adults.

Adenosine Injection is not effective in converting rhythms other than PSVT, such as atrial flutter, atrial fibrillation, or ventricular tachycardia to normal sinus rhythm.

Hemodynamics

Adenosine is a potent vasodilator in most vascular beds, except in renal afferent arterioles and hepatic veins where it produces vasoconstriction. The intravenous bolus dose of 6 or 12 mg Adenosine Injection usually has no systemic hemodynamic effects. When larger

doses are given by infusion, adenosine decreases blood pressure by decreasing peripheral resistance.

Pharmacokinetics

Intravenously administered adenosine is rapidly cleared from the circulation via cellular uptake, primarily by erythrocytes and vascular endothelial cells, with a half-life of less than 10 seconds. Intracellular adenosine is rapidly metabolized either via phosphorylation to adenosine monophosphate by adenosine kinase, or via deamination to inosine by adenosine deaminase in the cytosol. Adenosine monophosphate formed by phosphorylation of adenosine is incorporated into the high-energy phosphate pool. Inosine formed by deamination of adenosine can leave the cell intact or can be metabolized to hypoxanthine, xanthine and ultimately uric acid.

Since neither the kidney nor the liver are required for the metabolism or elimination of adenosine, the activity of Adenosine Injection should be unaffected by hepatic or renal insufficiency.

INDICATIONS AND CLINICAL USE

Adenosine Injection is indicated for the conversion to sinus rhythm of paroxysmal supraventricular tachycardia (PSVT), including that associated with accessory bypass tracts (Wolff-Parkinson-White Syndrome). When clinically advisable, appropriate vagal maneuvers (e.g. Valsalva maneuver) should be attempted prior to Adenosine Injection administration.

Adenosine Injection is indicated to aid in the diagnosis of broad or narrow complex supraventricular tachycardia. Although Adenosine Injection is not effective in converting atrial flutter, atrial fibrillation or ventricular tachycardia to sinus rhythm, the transient atrioventricular nodal block produced helps diagnosis of atrial activity.

It is essential to ascertain that Adenosine Injection actually reaches the systemic circulation (see **DOSAGE AND ADMINISTRATION**).

Adenosine Injection does not convert atrial flutter, atrial fibrillation or ventricular tachycardia to normal sinus rhythm.

Adenosine Injection should only be used with appropriate cardiac monitoring.

CONTRAINDICATIONS

Adenosine Injection is contraindicated in:

- Second or third degree AV block (except in patients with a functioning artificial pacemaker).
- Sick sinus syndrome (except in patients with a functioning artificial pacemaker).
- Symptomatic bradycardia (except in patients with a functioning artificial pacemaker).
- Known hypersensitivity to adenosine.

WARNINGS

Heart Block

Adenosine Injection exerts its effect by decreasing conduction through the A-V node and may produce a short lasting first-, second- or third-degree heart block. Appropriate therapy should be instituted as needed. Patients who develop high level block on one dose of Adenocard should not be given additional doses. Because of the very short half-life of adenosine (<10 seconds), these effects are generally self-limiting. Appropriate resuscitative measures should be available.

Rarely, ventricular fibrillation/flutter has been reported following Adenosine Injection administration, including both resuscitated and fatal events. In most instances, these cases were associated with the concomitant use of digoxin **and, less frequently with digoxin and verapamil**. Adenosine Injection should be used with caution in patients receiving digoxin **or digoxin and verapamil in combination**.

Patients with atrial fibrillation/flutter and an accessory by-pass tract may develop increased conduction down the anomalous pathway.

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, polymorphic ventricular tachycardia, torsades de pointes, atrial premature contractions, atrial fibrillation, sinus bradycardia, sinus tachycardia, skipped beats, and varying degrees of A-V nodal block. These arrhythmias and conduction disturbances were observed in about 55% of patients.

Asystole

Transient or prolonged episodes of asystole have been reported with fatal outcomes in some cases.

Bronchoconstriction

Adenosine Injection has been administered to a limited number of patients with asthma and serious exacerbation of their symptoms has been reported in some patients. Respiratory compromise has occurred during adenosine infusion in patients with chronic obstructive pulmonary disease (COPD). Therefore, the use of Adenosine Injection should be avoided in patients with COPD or asthma.

Adenosine Injection therapy should be discontinued in any patient who develops severe respiratory difficulties

PRECAUTIONS

Use in Pregnancy

Adenosine is a substance naturally present in the body and therefore no fetal effects would be anticipated. However, since it is not known whether Adenosine Injection can cause fetal harm when administered to pregnant women, it should not be used during pregnancy unless potential benefits outweigh the potential risks to the fetus.

Use in Children

No controlled studies have been conducted in pediatric patients to establish the safety and efficacy of Adenosine Injection for the conversion of paroxysmal supraventricular tachycardia (PSVT). However, open-label studies carried out by independent investigators indicated that intravenous adenosine can be used safely in neonates, infants, children and adolescents. (See Dosage and Administration - Pediatric Patients, and Selected Reference.)

Use in Elderly

Clinical studies of Adenosine Injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, Adenosine Injection in geriatric patients should

be used with caution since this population may have a diminished cardiac function, nodal dysfunction, concomitant diseases or drug therapy that may alter hemodynamic function and produce severe bradycardia or AV block.

Drug Interactions

1. **Cardioactive Drugs**
   Adenosine Injection has been effectively administered in the presence of other cardioactive drugs, such as quinidine, beta-adrenergic blocking agents, calcium channel blocking agents and angiotensin converting enzyme inhibitors, without any change in the adverse reaction profile. Digoxin and verapamil use may be rarely associated with ventricular fibrillation when combined with Adenosine Injection (see WARNINGS). Because of the synergistic depressant effects on the SA and AV nodes, Adenosine Injection should be used with caution in the presence of these agents.

2. **Methylxanthines**
   The effects of adenosine are antagonized by methylxanthines (such as caffeine and theophylline). In the presence of methylxanthines, larger doses of adenosine may be required or adenosine may not be effective.

3. **Dipyridamole**
   Adenosine effects are potentiated by dipyridamole. Thus, smaller doses of adenosine may be effective in the presence of dipyridamole.

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

ADVERSE REACTIONS

In controlled clinical trials 268 patients received Adenosine Injection. One hundred and two patients (38%) experienced one or more adverse events. These adverse events appeared immediately after administration of adenosine and usually lasted less than one minute. The most common adverse reactions were: facial flushing (18%), dyspnea (12%), chest pressure (7%) and nausea (3%).

Cardiovascular:
Facial flushing (18%), headache (2%), sweating, palpitations, chest pain, hypotension (less than 1%). A variety of arrhythmias and conduction disturbances were observed in about 55% of patients at the time of conversion to normal sinus rhythm.

Respiratory:
Shortness of breath/dyspnea (12%), chest pressure (7%), hyperventilation, head pressure (less than 1%).

Central Nervous System:
Lightheadedness (2%), dizziness, tingling in arms, numbness (1%), apprehension, blurred vision, burning sensation, heaviness in arms, neck and back pain (less than 1%).

Gastrointestinal:
Nausea (3%), metallic taste, tightness in throat, pressure in groin (less than 1%).

The following adverse events have been reported from marketing experience with Adenosine Injection. Because these events are reported voluntarily from a population of uncertain size, are associated with concomitant diseases and multiple drug therapies and surgical procedures, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Decisions to include these events in labeling are typically based on one or more of the following factors: (1) seriousness of the event, (2) frequency of the reporting, (3) strength of causal connection to the drug, or a combination of these factors.

Cardiovascular: Prolonged asystole, ventricular tachycardia, ventricular fibrillation, transient increase in blood pressure, bradycardia, atrial fibrillation, and Torsade de Pointes (See Warnings and Precautions).

Respiratory: Bronchospasm

Central Nervous System: Convulsions, grand mal and tonic clonic seizures

SYMPTOMS AND TREATMENT OF OVERDOSAGE

For management of a suspected overdose, please contact your regional Poison Control Centre.

No cases of overdosage associated with the use of Adenosine Injection have been reported. It is unlikely that the true overdosage will occur because adenosine has a short

half-life (<10 seconds) and Adenosine Injection is dosed by a rapid bolus injection. If prolonged adverse events associated with the use of Adenosine Injection occur, treatment should be individualized and directed toward the specific event. To date, no patient has required administration of adenosine antagonists such as aminophylline to counteract adverse events associated with the use of Adenosine Injection.

In clinical studies on the use of adenosine as a diagnostic agent in imaging, less than 0.1% of the patients exposed to adenosine were described as having severe, prolonged, adverse events. These prolonged adverse events were treated with aminophylline after discontinuation of the adenosine infusion. The usual concentration of aminophylline used was 1.25 mg/mL (125 mg in 100 mL) administered intravenously over five to six minutes. An additional 1.25 mg/mL (125 mg in 100 mL) can be administered, but clinical experience has demonstrated that this is rarely required.

DOSAGE AND ADMINISTRATION

Adenosine Injection should only be used with appropriate cardiac monitoring.

ADENOSINE INJECTION SHOULD BE GIVEN AS A RAPID BOLUS INTRAVENOUS INJECTION. TO BE CERTAIN THE SOLUTION REACHES THE SYSTEMIC CIRCULATION, IT SHOULD BE ADMINISTERED EITHER DIRECTLY INTO A PERIPHERAL VEIN OR, IF GIVEN INTO AN IV LINE, IT SHOULD BE GIVEN AS CLOSE TO THE PATIENT AS POSSIBLE AND FOLLOWED BY A RAPID SALINE FLUSH.

Adult Patients

The recommended intravenous doses for adults are as follows:

Initial dose:	6 mg administered as a rapid intravenous bolus given over a 1-2 second time period.
Additional doses:	If the initial dose does not terminate supra-ventricular tachycardia within 1-2 minutes, 12 mg dose should be given as a rapid intravenous bolus. This 12 mg dose may be repeated a second time if required. Single bolus injections greater than 12 mg are not recommended.

Pediatric Patients

Pediatric patients with a body weight < 50 kg:

Initial Dose:	Give 0.05-0.10 mg/kg as a rapid intravenous bolus given either centrally or peripherally.
Additional Doses:	If conversion of PSVT does not occur within 1-2 minutes, additional bolus injections of adenosine can be administered at incrementally higher doses, increasing the amount given by 0.05-0.10 mg/kg. Follow each bolus with a saline flush. This process should be continued until sinus rhythm is established or up to a maximum dose of 0.3 mg/kg.

For pediatric patients who require single intravenous doses less than 0.6 mg (0.2 mL), Adenosine Injection may be further diluted with normal saline to a final concentration range from 0.3 to 1 mg/mL.

Patient with a body weight ≥ 50 kg:

Administer the adult dose.

Single bolus injections greater than 12 mg are not recommended for adult or pediatric patients.

NOTE: Adenosine Injection should be inspected visually for particulate matter and discoloration prior to administration.

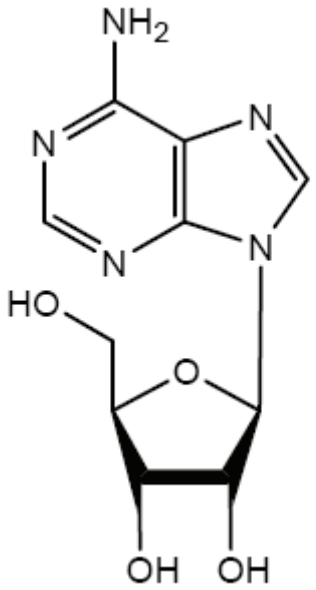
Adenosine Injection should not be refrigerated as crystallization may occur. If crystallization has occurred, dissolve crystals by warming to room temperature. The solution must be clear at the time of use.

PART II: SCIENTIFIC INFORMATION

PHARMACEUTICAL INFORMATION

Drug Substance

Structural formula:



Common Name: Adenosine

Chemical Name: 6-amino-9-β-D-ribofuranosyl-9-H-purine; Adenine riboside

Molecular Weight: 267.2 g/mol

Molecular Formula: $C_{10}H_{13}N_5O_4$

Description:

Adenosine is a white crystalline powder. It is soluble in water (7 mg/mL at pH 7.0) and practically insoluble in alcohol. Solubility increases by warming and by lowering the pH. The melting point is 233- 238^{0}C.

Composition:

Adenosine Injection is a sterile solution for rapid bolus intravenous injection and is available in 6 mg/2 mL prefilled syringes. Each mL contains 3 mg Adenosine and 9 mg Sodium Chloride in Water for Injection. The pH of the solution is between 4.5 and 7.5. Adenosine Injection does not contain preservatives, colours or additives.

The plastic syringe is molded from a specially formulated polypropylene. Water permeates from inside the container at an extremely slow rate which will have an insignificant effect on solution concentration over the expected shelf life. Solution in contact with the plastic container may leach out certain chemical components from the plastic in very small amounts; however, biological testing was supportive of the safety of the syringe material.

Stability and Storage Recommendations:

Adenosine Injection is supplied as a sterile non-pyrogenic solution in normal saline and should be stored at controlled room temperature 15ºC - 30º C. DO NOT REFRIGERATE as crystallization may occur. If crystallization has occurred, dissolve crystals by warming to room temperature. The solution must be clear at the time of use.

Availability of Dosage Forms:

Adenosine Injection is supplied in 6 mg in 2 mL (fill volume) Plastic disposable syringes, in a package of one.

Instructions for Syringe Use:

The new syringe delivery system, easily adapts to most peripheral line connection valves without the use of a needle. A needle is not provided with the Adenosine Injection flint glass syringe delivery system. Should you require the use of a needle to inject Adenosine Injection directly into a vein, the adaptable Luer Lock tip can accomodate an 18 or 20 gauge needle. To use the syringe, remove luer cover. Hold plunger and push barrel forward to relieve any resistance that may be present. Pull the barrel down until air is expelled from the syringe. Adenosine Injection is now ready to be administered. (See DOSAGE AND ADMINISTRATION Section). Syringes are intended for **single use** only. To prevent needle stick injuries needles should not be recapped, purposely bent or broken by hand. It is a latex free, plastic delivery system. Any portion of the syringe not used at once should be discarded. For additional information pertaining to the use of the Adenosine Injection syringe, please refer to the drug carton diagrams.

PHARMACOLOGY

A. Animal Studies

Cardiac Electrophysiology

Adenosine exerts pronounced negative chronotropic and dromotropic effects on cardiac pacemakers and atrioventricular (A-V) nodal conduction, respectively.

Junctional pacemakers appear to be more sensitive to adenosine than sinus pacemakers, and ventricular pacemakers more sensitive than junctional pacemakers.

Significant species variability was observed in animal experiments with regard to adenosine effects on the heart. In the guinea pig, the A-V node is more sensitive to adenosine then the sinus node, while the opposite is true in the dog. Dipyridamole potentiates the action of adenosine in the guinea pig, but not in the rat heart. Species variability has also been observed with regard to the indirect anti-adrenergic action of adenosine.

Acute Cardiovascular Effects of Adenosine

Adenosine was administered intravenously to three conscious male beagle dogs at an initial dose of 4.8 mg/kg and a second dose, administered 2-3 hours later, of 9.6 mg/kg. All dogs were observed for seven days. Examinations conducted both pre and post injection demonstrated no electrocardiographic changes.

Other Effects

Adenosine can induce bronchoconstriction in rats.

Increased levels of intrarenal adenosine caused a significant decrease in glomerular filtration rate, sodium excretion and renin release. Direct administration of adenosine into the cerebral ventricles resulted in ataxia, muscular weakness, sleepiness and change in behaviour.

Adenosine modulates sympathetic neurotransmission through actions at various sites including ganglia, presynaptic noradrenergic nerve terminals and postsynaptic target organs receiving sympathetic innervation. Adenosine can also affect cholinergic neurotransmission.

Pharmacokinetics

Adenosine is a naturally occurring nucleoside which is present in various forms in all cells of the body. Any intravenously administered dose of adenosine is minute in comparison to the existing body pool.

Adenosine may be converted to its base adenine and then to AMP, or directly to AMP. Adenosine may also be deaminated to inosine and then converted to AMP. Under normal circumstances adenosine is generated by breakdown of ATP and by biosynthesis in the liver. The biochemical pathways seem to be the same for all species. It appears that erythrocytes serve as the transporting vehicle for adenosine.

A system exists to conserve and recycle adenosine in the body. The major components of this salvage system appear to be the endothelial cells of the blood vessels and the erythrocytes themselves.

B. Human Studies

Adenosine at a dose of 83 μg/kg terminated electrically induced PSVT. However, it was ineffective in terminating either intraatrial tachycardia or atrial fibrillation (AF).

Bolus injections of adenosine, ranging from 3 to 12 mg, exert negative chronotropic and dromotropic effects on sinoatrial and atrioventricular nodes, respectively, without significant changes in blood pressure.

Continuous intravenous infusion, for 6 minutes, of 10-140 μg/kg/min in conscious human subjects resulted in increased heart rate (by 33 beats/min), increased systolic blood pressure (by 13 mmHg) and decreased diastolic blood pressure (by 8 mmHg). In addition, it caused pronounced increases in plasma norepinephrine and epinephrine levels.

When adenosine 70-90 μg/kg/min infusion was administered to conscious human subjects, both heart rate and skin temperature increased without a change in the blood pressure.

Systemic infusion of adenosine at dosages that affect myocardial blood flow, 40-50 μg/kg/min, had no effect on glomerular filtration rate or total renal blood flow in healthy subjects.

Inhalation of adenosine caused a concentration dependent bronchoconstriction in asthmatic patients, but not in non-asthmatics.

Adenosine Injection is a respiratory stimulant (probably through activation of carotid body chemoreceptors) and intravenous administration in man has been shown to increase minute ventilation (Ve) and reduce arterial PCO_2 causing respiratory alkalosis.

The short half-life of intravenously administered adenosine of less than 10 seconds makes it impossible to perform the standard pharmacokinetic studies in man.

TOXICOLOGY

Acute Single Dose Intravenous Toxicity

Adenosine was administered as a single intravenous injection to five male and five female Charles River CD-1 mice at a dose of 6 mg per animal, and to five male and five female Sprague-Dawley rats at a dose of 12 mg per animal.

No mortalities and no visible abnormalities or post-mortem abnormalities were observed in these studies.

The LD50 value was estimated to be greater than 240 mg/kg in mice and greater than 48 mg/kg in rats.

Acute Multi-Dose Intravenous Toxicity

a) Rats

Adenosine was administered intravenously to 10 male and 10 female Charles River CD rats at a dosage level of 200 mg/kg. Total dosage was administered in five approximately equal amounts, one minute apart. Control group received the vehicle.

Immediately following drug administration, most animals exhibited decreased activity which persisted for approximately 30 minutes. In addition, ataxia was observed in some animals. Four hours post dose, all surviving animals appeared normal.

One female from the treated group was found dead at the 30 minute observation interval. Prostration was noted prior to death. Red foci were observed in the thymus and left lobe of the lung of this animal. All other animals survived to study termination.

b) Dogs

Adenosine was administered intravenously to four male and four female beagle dogs at a dosage of 50 mg/kg. Total dosage was administered in five approximately equal amounts one minute apart. Control group received the vehicle. Higher incidence of decreased activity and ptyalism was seen in the treated group during the first hour after dosing. All dogs survived to study termination.

Long Term Toxicity and Carcinogenicity

Because adenosine is administered as a single dose and because it is a normal component of the body, no chronic toxicity studies and no carcinogenicity studies were performed.

Mutagenicity

Adenosine was tested in the Salmonella/Mammalian Microsome Plate Incorporation Mutagenicity Assay for its ability to induce back mutations at selected loci of several strains of *Salmonella typhimurium* in the presence and absence of rat liver microsomal enzymes. The tester strains used were TA98, TA100, TA1535, TA1537 and TA1538. Adenosine did not cause a positive response in any of the tester strains either in the presence or absence of microsomal enzymes.

Reproduction and Teratology

Adenosine present at millimolar concentrations in cell cultures produces a variety of chromosomal alterations. In rats and mice, adenosine administered intraperitoneally once a day for five days at 50, 100 and 150 mg/kg [10-30 (rats) and 5-15 (mice) times human dosage on a mg/M^2 basis] caused decreased spermatogenesis and increased the number of abnormal sperm, a reflection of the ability of adenosine to produce chromosomal damage.

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PART III: CONSUMER INFORMATION

[Pr]Adenosine Injection, USP
(adenosine injection, USP, 3 mg/mL)

This leaflet is designed specially for Consumers. It is a summary and will not tell you everything about Adenosine Injection. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:
Adenosine Injection is a injectable medication used to treat a condition called paroxysmal supraventricular tachycardia (rapid rhythm of the heart), including a condition called Wolff-Parkinson-White Syndrome (abnormal electrical communication from the atria to the ventricles). These conditions cause your heart to beat too fast. Adenosine Injection helps your heart go back to a normal rhythm (stop beating too fast). Adenosine Injection is also used to help your doctor determine if you have an abnormal heart beat called broad or narrow supraventricular tachycardia.

What it does:
Adenosine, the active ingredient in Adenosine Injection, is a substance that occurs naturally in all cells of your body. Adenosine Injection works by slowing down the electrical impulses which control your heart rhythm. This allows your heart rhythm to return to normal.

When it should not be used:
You should not use Adenosine Injection if:
- You have had an allergic reaction to adenosine.
- 2. You have any of the following conditions, unless you have an artificial pacemaker that works:

1. A type of heart condition called second or third degree atrioventricular (AV) block,
2. An abnormal heart rhythm called sick sinus syndrome,
3. Bradycardia (a slow heart beat)

What the medicinal ingredient is:
Adenosine

What the non-medicinal ingredients are:
Sodium chloride, Water for Injection

What dosage forms it comes in:
Adenosine Injection is supplied in 6 mg per 2 mL (fill volume) in plastic disposable syringes, in a package of one.

WARNINGS AND PRECAUTIONS

BEFORE Adenosine Injection is given be sure to tell your doctor:
- If you have a history of heart problems such as heart block or atrial fibrillation/flutter (fast heart beat or palpitations)
- 2. If you have asthma or other lung diseases such as chronic obstructive pulmonary disease (COPD)
- 3. About all other health conditions you have now, or have had in the past
- If you are pregnant or plan to become pregnant

INTERACTIONS WITH THIS MEDICATION

Adenosine Injection and other medicines may interact with each other. Tell your doctor about all the medicines you take including prescription medicines, over the counter medicines, vitamins, and herbal supplements. In particular you should tell your doctor if you are taking any of the following:
- Digoxin
- 2. Verapamil
- 3. Methylxanthines, such as theophylline and caffeine (present in many foods and drinks such as coffee, tea and chocolate)
- Dipyridamole
- Carbamazepine

PROPER USE OF THIS MEDICATION

ADENOSINE INJECTION is given to patients by injection directly into the blood system. This drug should only be used in a setting with appropriate cardiac monitoring and resuscitative facility.

Usual dose:
For Adults and Children Over 50 kg
The initial dose is 6 mg. If this does not slow your heart rate, you may receive one or two more injections of 12 mg.
For Children Weighing Less Than 50 kg
The amount of drug given will depend on how much you weigh. If the first injection does not slow your heart rate, you may get more injections.

Overdose:
No cases of overdose associated with the use of Adenosine Injection have been reported. If you feel you have been given too much medication, discuss it with your doctor.

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Along with its intended action, any medication may cause undesirable effects.

The most common side effects of Adenosine Injection include facial flushing, dyspnea (shortness of breath), chest pressure, and nausea. These side effects start immediately after Adenosine Injection is given and usually last less than one minute.

Other side effects include:
Headache, sweating, palpitations, chest pain, hypotension (less than 1%), a variety of arrhythmias and conduction disturbances were observed in about 55% of patients at the time of conversion, hyperventilation, head pressure, lightheadedness, dizziness, tingling in arms, numbness, apprehension, blurred vision, burning sensation, heaviness in arms, neck and back pain, metallic taste, tightness in throat, pressure in groin.

In addition to the above reports, the below adverse events listed have been reported post marketing:

Prolonged asystole (cardiac arrest), transient increase in blood pressure and bronchospasm (sudden constriction of the muscles in the walls of bronchioles).

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or Pharmacist		Stop taking drug and seek immediate emergency medical attention
	Only if severe	In all cases	
Uncommon			
Difficulty breathing		√	
Unknown			
Seizures*		√	
Abnormal heart beat* (irregular, slow or fast)		√	

*Unable to determine frequency since this is a post- marketing event

This is not a complete list of side effects. For any unexpected effects while taking Adenosine Injection, contact your doctor

HOW TO STORE IT

Store at controlled room temperature between 15ºC to 30ºC. If crystallization has occurred, dissolve crystals by warming at room temperature.

DO NOT REFRIGERATE.
The solution must be clear at the time of use.

REPORTING SUSPECTED SIDE EFFECTS
You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

1. Report online at www.healthcanada.gc.ca/medeffect
2. Call toll-free at 1-866-234-2345
3. Complete a Canada Vigilance Reporting Form and:
   - Fax toll-free to 1-866-678-6789, or
   - Mail to: Canada Vigilance Program
     Health Canada
     Postal Locator 0701E
     Ottawa, Ontario
     K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document can be found at: www.mylan.ca.

The full Product Monograph prepared for health professionals can be obtained by contacting the sponsor, Mylan Pharmaceuticals ULC at: 1-800-575-1379

This leaflet was prepared by Mylan Pharmaceuticals ULC
Etobicoke, Ontario M8Z 2S6

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Mylan

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