Prescription only medicines

CARDIOSIN

Adenosine Injection USP 3 mg/ml, 2 ml
For Rapid IV Use Only
Solution for Injection

Composition:
Each ml Contains:
Adenosine USP … 3 mg
Sodium Chloride BP … 9 mg
Water for Injections BP … q.s.

THERAPEUTIC INDICATIONS

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

Paediatric population

Rapid conversion to a normal sinus rhythm of paroxysmal supraventricular tachycardia in children aged 0 to 18 years.

Diagnostic Indications

Aid to diagnosis of broad or narrow complex supraventricular tachycardias. Although adenosine injection will not convert atrial flutter, atrial fibrillation or ventricular tachycardia to sinus rhythm, the slowing of AV conduction helps diagnosis of atrial activity.
Sensitisation of intra-cavitary electrophysiological investigations.

POSOLOGY AND METHOD OF ADMINISTRATION

Adenosine is intended for hospital use only with monitoring and cardiorespiratory resuscitation equipment available for immediate use.

Method of administration

Adenosine should be administered by rapid intravenous (IV) bolus injection into a vein or into an IV line. If given into an IV line it should be injected through as proximally as possible, and followed by a rapid saline flush. If administered through a peripheral vein, a large bore cannula should be used.
During administration of adenosine cardio-respiratory resuscitation equipment must be available for immediate use if necessary.
Adenosine is intended for use with continuous monitoring and ECG recording during administration.
Patients who develop high-level AV block at a particular dose should not be given further dosage increments.

Posology

Adults:

Initial dose: 3mg 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 1 to 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 12mg should be given also as a rapid intravenous bolus.
Additional or higher doses are not recommended.

Paediatric population

During administration of adenosine cardio-respiratory resuscitation equipment must be available for immediate use if necessary.
Adenosine is intended for use with continuous monitoring and ECG recording during administration.
The dosing recommended for the treatment of paroxysmal supraventricular tachycardia in the paediatric population is:
-first bolus of 0.1 mg/kg body weight (maximum dose of 6mg)
-increments of 0.1 mg/kg body weight as needed to achieve termination of supraventricular tachycardia (maximum dose of 12mg).

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.

CONTRAINDICATIONS

Adenosine injection is contraindicated for patients presenting:
• Known hypersensitivity to adenosine or to any of the excipients.
• Sick sinus syndrome, second or third degree Atrio-Ventricular (AV) block (except in patients with a functioning artificial pacemaker).
• Chronic obstructive lung disease with evidence of bronchospasm (e.g. asthma bronchiale)
• Long QT syndrome.
• Severe hypotension;
• Decompensated states of heart failure.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Special warnings:

Due to the possibility of transient cardiac arrhythmias arising during conversion of the supraventricular tachycardia to normal sinus rhythm, administration should be carried out in a hospital setting with monitoring and cardio-respiratory resuscitation equipment available for immediate use if necessary. During administration, continuous ECG monitoring is necessary as life-threatening arrhythmia might occur.
Because it has the potential to cause significant hypotension, adenosine injection should be used with caution in patients with left main coronary stenosis, uncorrected hypovolemia, stenotic valvular heart disease, left to right shunt, pericarditis or pericardial effusion, autonomic dysfunction or stenotic carotid artery disease with cerebrovascular insufficiency. There have been reports of cerebrovascular accident/transient ischemic attack, secondary to the haemodynamic effects of adenosine.
There have been reports of myocardial infarction shortly after use of Adenosine. Adenosine should be used with caution in patients with recent myocardial infarction, severe heart failure, or in patients with minor conduction defects (first degree A-V block, bundle branch block) that could be transiently aggravated during infusion.
Adenosine 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.
Rare cases of severe bradycardia have been reported. Some occurred in early post- transplant patients; in the 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, especially in patients with prolonged QT intervals.
In patients with recent heart transplantation (less than 1 year) an increased sensitivity of the heart to adenosine has been observed.
Since neither the kidney nor the liver are involved in the degradation of exogenous adenosine, adenosine injection's efficacy should be unaffected by hepatic or renal insufficiency.
As dipyridamole is a known inhibitor of adenosine uptake, it may potentiate the action of adenosine injection. It is therefore suggested that adenosine injection should not be administered to patients receiving dipyridamole; if use of Adenosine Injection is essential, dipyridamole should be stopped 24 hours before hand, or the dose of Adenosine Injection should be greatly reduced.

Precautions:

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.
Adenosine may trigger convulsions in patients who are susceptible to convulsions. In patients with history of convulsions/seizures, the administration of adenosine should be carefully monitored.
Because of the possible risk of torsades de pointes, adenosine injection should be used with caution in patients with a prolonged QT interval, whether this is drug induced or of metabolic origin. Adenosine injection is contraindicated in patients with Long QT syndrome.
Adenosine may precipitate or aggravate bronchospasm.
Adenosine injection contains approximately 7mg sodium per injection vial (2ml) i.e. essentially 'sodium-free'.

Paediatric population

Adenosine may trigger atrial arrhythmias and thus might lead to ventricular acceleration in children with Wolff-Parkinson-White (WPW) syndrome.
The efficacy of intraosseus administration has not been established.

INTERACTION WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Dipyridamole inhibits adenosine cellular uptake and metabolism, and potentiates the action of adenosine. In one study dipyridamole was shown to produce a 4-fold increase in adenosine actions. Asystole has been reported following concomitant administration.
It is therefore suggested that adenosine injection should not be administered to patients receiving dipyridamole; if use of adenosine injection is essential, dipyridamole should be stopped 24 hours before hand, or the dose of adenosine should be greatly reduced.
Aminophylline, theophylline and other xanthines are competitive adenosine antagonists and should be avoided for 24 hours prior to use of adenosine.
Food and drinks containing xanthines (tea, coffee, chocolate and cola) should be avoided for at least 12 hours prior to use of adenosine injection.
Adenosine may interact with drugs tending to impair cardiac conduction.

PREGNANCY AND LACTATION

Pregnancy:

There are no or limited amount of data from the use of adenosine in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. Adenosine is not recommended during pregnancy unless the physician considers the benefits to outweigh the potential risks.

Breast Feeding:

It is unknown whether adenosine metabolites are excreted in human milk
Adenosine Injection should not be used during breast-feeding.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Not applicable

UNDESIRABLE EFFECTS

These side effects are generally mild, of short duration (usually less than 1 minute) and well tolerated by the patient. However severe reactions can occur.
Methylxanthines, such as IV aminophylline or theophylline have been used to terminate persistent side effects (50 – 125 mg by slow intravenous injection).
Adverse events are ranked under the heading of the frequency:
Very common (>1/10), Common (>1/100, <1/10), Uncommon (>1/1,000, <1/100), Rare (>1/10,000, <1/1,000), Very rare (<1/10,000), Not known (cannot be estimated from available data).

Immune system disorders:

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

Cardiac disorders:

Very common: bradycardia, sinus pause, skipped beats, atrial extrasystoles, Atrio-Ventricular block, ventricular excitability disorders such as ventricular extrasystoles, non-sustained ventricular tachycardia
Uncommon: sinus tachycardia, palpitations
Very rare: atrial fibrillation, severe bradycardia not corrected by atropine and possibly requiring temporary pacing, ventricular excitability disorders, including ventricular fibrillation and torsade de pointes.
Not known: asystole/cardiac arrest, sometimes fatal especially in patients with underlying ischemic heart disease/cardiac disorder, arteriospasm coronary which may lead to myocardial infarction.

Vascular disorders:

Very common: flushing
Not known: hypotension (sometimes severe)

Nervous system disorders:

Common: headache, dizziness, light-headedness, paraesthesia
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

Eye disorders:

Uncommon: blurred vision

Respiratory, thoracic and mediastinal disorders:

Very common: dyspnea (or the urge to take a deep breath)
Uncommon: hyperventilation
Very rare: bronchospasm
Not known: respiratory failure, apnea/respiratory arrest
Cases of respiratory failure, bronchospasm, apnea, and respiratory arrest with fatal outcome have been reported.

Gastrointestinal disorders:

Common: nausea
Uncommon: metallic taste
Not known: vomiting

Psychiatric disorders:

Common: nervousness

General disorders and administration site conditions:

Very common: chest pain or pressure, feeling of thoracic constriction/oppression
Common: burning sensation
Uncommon: sweating, discomfort in the leg, arm or back, feeling of general discomfort, weakness/pain
Very rare: injection site reactions

OVERDOSE

Overdose would cause severe hypotension, bradycardia or asystole. The half-life of adenosine in blood is very short, and side effects (when they occur) would quickly resolve. Administration of IV aminophylline or theophylline may be needed. Pharmacokinetic evaluation indicates that methyl xanthines are competitive antagonists to adenosine, and that therapeutic concentrations of theophylline block its exogenous effects.

PHARMACOLOGICAL PROPERTIES

PHARMACODYNAMICS PROPERTIES

ATC Code: Other Cardiac Preparations **C01EB 10**

Endogenous nucleoside with peripheral vasodilator/antiarrhythmic effect
Antiarrhythmic drug Adenosine is a purine nucleoside which is present in all cells of the body. Animal pharmacology studies have in several species shown that Adenosine has a negative dromotropic effect on the atrioventricular (AV) node.
In man adenosine administered by rapid intravenous injection slows 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. Once the circuit has been interrupted, the tachycardia stops and normal sinus rhythm is re-established.
One acute interruption of the circuit is usually sufficient to arrest the tachycardia.
Since atrial fibrillation and atrial flutter do not involve the AV node as part of a re-entry circuit, Adenosine will not terminate these arrhythmias.
By transiently slowing AV conduction, atrial activity is easier to evaluate from ECG recordings and therefore the use of adenosine can aid the diagnosis of broad or narrow 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.
Paediatric population
No controlled studies have been conducted in paediatric patients with adenosine for the conversion of paroxysmal supraventricular tachycardia (PSVT). However, the safety and efficacy of adenosine in children aged 0 to 18 years with PSVT is considered established based on extensive clinical use and literature data (open label studies, case reports, clinical guidelines). Literature review identified 14 studies where IV adenosine was used for acute termination of supraventricular tachycardia (SVT) in around a total of 450 paediatric patients aged 6 hours to 18 years. Studies were heterogenic in terms of age, and dosing schedules. SVT was terminated in 72 to 100% of cases in most of the published studies. Dosages used varied from 37.5 mcg/kg to 400 mcg/kg. Several studies discussed a lack of response to starting doses less than 100mcg/kg.
Depending on the child's clinical history, symptoms and ECG diagnosis, adenosine has been used in clinical practice under expert supervision in children with stable wide-QRS complex tachycardia and Wolff-Parkinson- White syndrome however the currently available data does not support a paediatric indication. In total 6 cases of adenosine-induced arrhythmias (3 atrial fibrillation, 2 atrial flutter, 1 ventricular fibrillation) have been described in 6 children aged 0 to 16 years with manifest or concealed WPW syndrome, of which 3 spontaneously recovered and 3 needed amiodarone +/- cardioversion.
Adenosine has been used as an aid to diagnosis of broad or narrow complex supraventricular tachycardias in same doses as for treatment of supraventricular tachycardia. Although adenosine will not convert atrial flutter, atrial fibrillation or ventricular tachycardia to sinus rhythm, the slowing of AV conduction helps diagnosis of atrial activity. However, the currently available data does not support a paediatric indication for the use of adenosine for diagnostic purposes.

PHARMACOKINETIC PROPERTIES

It is impossible to study adenosine in classical pharmacokinetic studies. It is present in various forms in all cells of the body where it plays an important role in energy production and utilisation systems. An efficient salvage and recycling system exist in the body, primarily in the erythrocytes and blood vessel endothelial cells. The half-life in vitro is estimated to be less than 10 seconds. The in vivo half-life may be even shorter.

PRECLINICAL SAFETY DATA

There are no pre-clinical data of relevance to the prescriber that are additional to those already included in other sections of the SPC.

INCOMPATIBILITIES

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

Do not use if any particles or discoloration are noticed in the solution.
Any unused product or waste material should be disposed of in accordance with local requirements.

STORAGE CONDITION: Store below 30°C. Protect from Light.

KEEP OUT OF REACH THE CHILDREN

DOSAGE FORM AND PACKING STYLE:

Dosage Form: Solution for Injection
Packing Style: Available in glass Vial.

Manufactured by:
SWISS PARENTERAL LTD.
Ahmedabad, Gujarat, INDIA

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