Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Adenosine 3 mg/ml solution for injection in pre-filled syringe

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 ml solution contains 3 mg of adenosine.

Each 1 ml single dose pre-filled syringe contains 3 mg of adenosine.
Each 2 ml single dose pre-filled syringe contains 6 mg of adenosine.
Each 4 ml single dose pre-filled syringe contains 12 mg of adenosine.

Each 1 ml of solution contains 3.54 mg (0.15 mmoL) of sodium

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection in pre-filled syringe
Clear, colourless solution.

pH: 5.5 – 7.5
Osmolality: 270 – 330 mOsm/kg

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

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

Diagnostic Indications
Aid to diagnosis of broad or narrow complex supraventricular tachycardias. 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.

Sensitisation of intra-cavitary electrophysiological investigations.

4.2 Posology and method of administration

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

Adenosine 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.

Posology
Adult:
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
These pre-filled syringes are not suitable for paediatric use.

Older people
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:
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.

4.3 Contraindications

Adenosine is contraindicated for patients presenting:
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- 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.

4.4 Special warnings and precautions for use

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 (see section 4.2).

Because it has the potential to cause significant hypotension, adenosine 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.

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 heart 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'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. It is therefore suggested that adenosine should not be administered to patients receiving dipyridamole; if use of adenosine is essential, dipyridamole should be stopped 24 hours before hand, or the dose of Adenosine should be greatly reduced. (*see Section 4.5 Interactions with other Medicaments and other forms of Interaction*).

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 should be used with caution in patients with a prolonged QT interval, whether this is drug induced or of metabolic origin. Adenosine Kabi is contraindicated in patients with long QT syndrome (see section 4.3).

Adenosine may precipitate or aggravate bronchospasm (see sections 4.3 and 4.8).

The efficacy of intraosseus administration has not been established.

Adenosine contains approximately 9 mg sodium chloride per ml. (corresponding to 3.54 mg sodium per ml). To be taken into consideration by patients on a controlled sodium diet.

4.5 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 should not be administered to patients receiving dipyridamole; if use of adenosine is essential, dipyridamole should be stopped 24 hours before hand, or the dose of adenosine should be greatly reduced. *See Section 4.4 Special Warnings and Precautions for Use.*

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.

Adenosine may interact with drugs tending to impair cardiac conduction.

4.6 Fertility, 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 should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

Adverse events are ranked under the heading of the frequency:

Very common (≥1/10), Common (≥1/100, <1/10), Uncommon (≥1/1000, <1/100), Rare (≥1/10000, <1/1000), Very rare (<1/10000), Not known (cannot be estimated from available data).

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).

Frequency	***Applicable to Adenosine 3mg/ml***
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 (see section 4.4)
Not known	- Hypotension sometimes severe - Asystole /Cardiac arrest, sometimes fatal especially in patients with underlying ischemic heart disease /cardiac disorder (see section 4.4) - Arteriospasm coronary which my lead to myocardial infarction
Nervous System disorders	
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 (see section 4.4)
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 (see section 4.4)
Not known	- Respiratory failure (see section 4.4) - 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
Vascular disorders	
Very common	- Flushing
General disorders and Administration Site conditions	
Very common	- Chest pressure/pain, feeling of thoracic constriction/oppression
Common	- Burning sensation
Uncommon	- Sweating - Feeling of general discomfort / weakness / pain
Very rare	- Injection site reactions
Psychiatric disorders	
Common	- Apprehension
Immune system disorders	

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

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance. Website: www.hpra.ie

4.9 Overdose

Overdosage 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other Cardiac Preparations: ATC Code: C01EB 10

Endogenous nucleoside with peripheral vasodilator/antiarrhythmic effect

Antiarrhythmic drug.

Mechanism of action:
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.

5.2 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 exists 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.

5.3 Preclinical safety data

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Water for injections

6.2 Incompatibilities

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

6.3 Shelf life

36 months.
The product should be used immediately after opening.

6.4 Special precautions for storage

Do not refrigerate.

6.5 Nature and contents of container

1 ml plastic pre-filled syringe containing 1 ml (3mg/1ml) closed with a halobutyl tip cap. No needle is present.
Packs containing:
1 pre-filled syringe
6 pre-filled syringes
10 pre-filled syringes

5 ml plastic pre-filled syringe containing 2 mL (6 mg/2 ml) closed with a halobutyl tip cap . No needle is present.
Packs containing:
1 pre-filled syringe
6 pre-filled syringes
10 pre-filled syringes

5 ml plastic pre-filled syringe containing 4 ml (12 mg/4 ml) closed with a halobutyl tip cap. No needle is present.
Packs containing:
1 pre-filled syringe
6 pre-filled syringes
10 pre-filled syringes

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

When using the 5 ml pre-filled syringe containing 4 ml (12 mg adenosine/4 ml) to administer only a 6 mg dose, 2 ml must be first discarded from the syringe before administering the remaining 2 ml to the patient.

Do not use if any particles or discolouration are noticed in the solution.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

Instructions for use of pre-filled syringe:

Use Aseptic Technique

1. Remove tip cap

2. Hold plunger and push barrel forward to relieve any resistance that may be present.

3. Pull the barrel down until air is expelled from the syringe.

7 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1
Bad Homburg v.d.H 61352
Germany

8 MARKETING AUTHORISATION NUMBER

PA2059/004/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 28th August 2015
Date of last renewal: 20th July 2020

10 DATE OF REVISION OF THE TEXT

February 2024