Approved Professional Information for ADENOCOR®

SCHEDULING STATUS

S4

1. NAME OF THE MEDICINE

ADENOCOR® 6 mg/2 mL solution for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains adenosine [(R)-1-(6-amino-9H-purin-9yl)-1-deoxy-D-ribofuranose] 6 mg per 2 mL (3 mg/mL).

Sugar free.

For the full list of excipients, see section 6 .1.

3. PHARMACEUTICAL FORM

Solution for injection.

Clear, colourless solution in a clear glass vial.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Conversion to sinus rhythm of paroxysmal supraventricular tachycardia, including those associated with accessory bypass tracts (Wolff-Parkinson-White syndrome).

4.2 Posology and method of administration

ADENOCOR should only be used when facilities exist for cardiac monitoring and resuscitation. 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, administer either directly into a vein or into an IV line. If given into an IV line, it should be injected as proximally as possible, and followed by a rapid saline flush.

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 elimination of the supraventricular tachycardia within 1 to 2 minutes, 6 mg 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, 12 mg should be given also as a rapid intravenous bolus. Additional or higher doses are not recommended.

Children: No controlled paediatric study has been undertaken.

Elderly: Dosage is as for adults.

4.3 Contraindications

ADENOCOR is contraindicated in patients suffering from:

- Known hypersensitivity to adenosine or to any of the excipients listed in section 6.1.
- 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).
- Chronic obstructive lung disease (such as asthma and COPD).
- Long QT syndrome.
- Severe hypotension; decompensated states of heart failure.

4.4 Special warnings and precautions for use

Because ADENOCOR has the potential to cause significant hypotension, ADENOCOR 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.

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. ADENOCOR 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.

Some 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 occurrence of torsades de pointes. In patients with recent heart transplantation (less than 1 year) an increased sensitivity of the heart to ADENOCOR has been observed.

ADENOCOR may precipitate or aggravate bronchospasm.

Dipyridamole inhibits ADENOCOR cellular uptake and metabolism, and potentiates the action of ADENOCOR. In one study dipyridamole was shown to produce a 4-fold increase in adenosine activity. If use of ADENOCOR bolus injection is judged to be essential, dipyridamole should be discontinued 24 hours beforehand, or the dose of ADENOCOR should be significantly reduced.

ADENOCOR is intended for use by health care professionals (medical practitioners and nurses) 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.

The use of ADENOCOR is contraindicated in patients receiving dipyridamole (see section 4.5). If use of adenosine bolus injection is judged to be essential, dipyridamole should be discontinued 24 hours beforehand, or the dose of adenosine should be significantly reduced.

ADENOCOR contains less than 1 mmol sodium (23 mg) per 2 mL vial, that is to say it is essentially sodium free.

4.5 Interaction with other medicines and other forms of interaction

Dipyridamole inhibits ADENOCOR cellular uptake and metabolism, and potentiates the action of ADENOCOR. In one study dipyridamole was shown to produce a 4-fold increase in adenosine activity. If use of ADENOCOR bolus injection is judged to be essential, dipyridamole should be discontinued 24 hours beforehand, or the dose of ADENOCOR should be significantly reduced.

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

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

ADENOCOR may interact with medicines tending to impair cardiac conduction.

Carbamazepine has been reported to increase the degree of heart block produced by other medicines. 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

Safety and efficacy in pregnancy and lactation have not been demonstrated.

ADENOCOR should not be used during lactation.

4.7 Effects on ability to drive and use machines

Because of its short duration of action, ADENOCOR should not influence a patient's ability to drive and to use machines.

Dizziness/light-headedness and blurred vision have been reported with ADENOCOR (see section 4.8). The patient's condition should be monitored before discharging.

4.8 Undesirable effects

Adverse reactions have been ranked under heading of system organ class and frequency using the following convention:

- very common: ≥ 10 %;
- common: ≥ 1 % and < 10 %;
- uncommon: ≥ 0,1 % and < 1 %;
- rare: ≥ 0,01 % and < 0,1 %;
- very rare: < 0,01 %;
- frequency unknown: 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.

Psychiatric disorders:

Common: apprehension.

Nervous system disorders:

Common: headache, dizziness/light-headedness.

Uncommon: head pressure.

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

Eye disorders:

Uncommon: blurred vision.

Cardiac disorders:

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

Uncommon: sinus tachycardia, palpitations.

Very rare: severe bradycardia which is not corrected by atropine and may require temporary pacing, atrial fibrillation, ventricular excitability including torsade de pointes and ventricular fibrillation (see section 4.4).

Respiratory, thoracic and mediastinal disorders:

Very common: dyspnoea (or the urge to take a deep breath).

Uncommon: hyperventilation.

Very rare: bronchospasm.

Gastrointestinal system disorders:

Common: nausea.

Uncommon: metallic taste.

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.

Post-marketing data:

The following adverse reactions have been reported however the frequencies are unknown:

Immune system disorders:

Anaphylactic reaction (including angioedema and skin reactions such as urticaria and rash).

Nervous system disorders:

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

Cardiac disorders:

Asystole/cardiac arrest, sometimes fatal; especially in patients with underlying ischaemic heart disease/cardiac disorder. MI/ST segment elevation, especially in patients with pre-existing severe coronary artery disease (see section 4.4)

Vascular disorders:

Hypotension, sometimes severe, cerebrovascular accident/transient ischaemic attack, secondary to the haemodynamic effects of adenosine including hypotension (see section 4.4).

Respiratory, thoracic and mediastinal disorders:

Respiratory failure (see section 4.4), apnoea/respiratory arrest.

Cases with fatal outcome of respiratory failure, of bronchospasm, and of apnoea/respiratory arrest have been reported.

Gastrointestinal system disorders:

Vomiting.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of ADENOCOR is important. It allows continued monitoring of the benefit/risk balance of ADENOCOR. Health care providers are asked to report any suspected adverse reactions to:

- The Pharmacovigilance Unit at Sanofi: za.drugsafety@sanofi.com (email) or 011 256 3700 (tel), or
- SAHPRA via the "**6.04 Adverse Drug Reaction Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

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 directed toward the specific symptom.

Methylxanthines, such as caffeine and theophylline, and aminophylline are competitive antagonists of adenosine.

Intravenous aminophylline or theophylline may be needed.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 6.2 Cardiac depressants.

Pharmacotherapeutic group: Cardiovascular system, cardiac therapy, other cardiac preparations.

ATC code: C01EB10.

ADENOCOR (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.

Neither the kidney nor the liver is involved in the degradation of exogenous adenosine.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride

Water for injection.

6.2 Incompatibilities

Compatibility with other medicines is not known.

6.3 Shelf life

Unopened vials:

36 months.

After first opening:

Use immediately.

6.4 Special precautions for storage

Store at or below 25 °C, protected from light.

Do not refrigerate.

6.5 Nature and contents of container

Clear glass vials with chlorobutyl rubber closures secured with aluminium caps, containing 6 mg adenosine per 2 mL. Packs of 6 vials on plastic trays in cardboard cartons.

6.6 Special precautions for disposal and other handling

For single use only. Any unused portion of the vial should be discarded.

7. HOLDER OF CERTIFICATE OF REGISTRATION

sanofi-aventis south africa (pty) ltd

Hertford Office Park, Building I, 5th Floor

90 Bekker Road, Vorna Valley

Midrand 2196

South Africa

8. REGISTRATION NUMBER

27/6.2/0467

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

1 September 1993

10. DATE OF REVISION OF THE TEXT

14 June 2023