PACKAGE LEAFLET:
INFORMATION FOR THE USER

Adenocor® 3mg/ml solution for injection
Adenosine

Sanofi

Is this leaflet hard to see or read?
Phone 01 4035600 for help
Read all of this leaflet carefully before you are given this medicine.
• Keep this leaflet. You may need to read it again
• If you have any further questions after reading this leaflet, ask your doctor
• If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor, nurse or pharmacist

In this leaflet:

1. What Adenocor is and what it is used for

Adenocor contains a medicine called adenosine. This belongs to a group of medicines called 'antiarrythmics'. Adenocor works by slowing down electrical impulses between the upper and lower chambers of the heart. This slows the fast or uneven heartbeats called 'arrythmias'.

Adenocor is used:
Adults
• During a test. This is to help doctors find out what type of arrythmia (uneven heartbeat) you have
• To bring your heart beat back to normal if you have a type of arrythmia called 'paroxysmal supraventricular tachycardia (SVT)' or 'Wolf-Parkinson-White Syndrome

Children:
• To bring your childs heart back to normal if your child has a type of heart rhythm trouble called 'paroxysmal supraventricular tachycardia' (PSVT).

2. What you need to know before you are given Adenocor

Do not have this medicine and tell your doctor if:
• You are allergic (hypersensitive) to adenosine or any of the other ingredients of Adenocor (listed in section 6 below). Signs of an allergic reaction include: a rash, swallowing or breathing problems, swelling of your lips, face, throat or tongue
• You have problems with your heart rhythm and do not have a pacemaker
• You have asthma

• You have been told you have ‘Long QT syndrome’. This is a rare heart problem that can lead to a fast heartbeat and fainting
• You have very low blood pressure (severe hypotension)
• You have heart failure where your heart is not pumping out enough blood
• Do not have this medicine if any of the above apply to you.

If you are not sure, talk to your doctor, nurse or pharmacist before you are given Adenocor.

Warnings and precautions
Take special care with Adenocor Check with your doctor, nurse or pharmacist before you have Adenocor if:
• You have a certain type of unusual heart rhythm (atrial fibrillation or atrial flutter) and in particular if you have an ‘accessory conduction pathway’
• You have any other severe breathing problem such as Chronic Obstructive Pulmonary Disease (COPD)
• You have been told that you have a heart problem whereby the electrical impulses in parts of your heart take longer than normal to discharge and then recharge (prolonged QT interval)
• You have low blood volume (hypovolaemia) that is not adequately corrected by treatment with medicines
• You have narrowing of the main arteries in the neck (carotid artery). This means that not enough blood is getting to the brain (cerebrovascular insufficiency)
• You have heart disease due to narrowing of
your heart valves (stenotic valvular heart
disease)
• You have inflammation of the membrane surrounding your heart (pericarditis) or a build up of fluid around your heart (pericardial effusion)
• You have a left-right shunt in your heart. This will mean blood goes directly from the left side of your heart to the right side
• You have narrowing of the left main artery supplying blood to your heart (left main coronary stenosis)
• You have had a recent heart attack, severe failure or you have had a transplant in the last year
• You have any minor problem with your heart (first degree AtrioVentricular block or bundle branch block). These conditions may be temporarily aggravated when you are given Adenocor
• If you have an abnormal heartbeat (atrial fibrillation or flutter)
• You have a problem with a part of your nervous system called "autonomic nervous system"

Taking or using other medicines
Please tell your doctor, nurse or pharmacist if you are taking or have recently taken any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because Adenocor can affect the way some other medicines work. Also some medicines can affect the way Adenocor works. In particular, check with your doctor, nurse or pharmacist if you are taking any of the following:
• Dipyridamole (medicine used to thin the blood). Make sure your doctor knows you are taking dipyridamole. Your doctor may decide you should not have Adenocor or may need to give you a lower dose of Adenocor
• Aminophylline or theophylline (medicines used to help breathing).
• Caffeine (sometimes found in headache medicines)

Taking Adenocor with food and drink
Food and drinks containing caffeine such as tea, coffee, chocolate and cola should be avoided for at least 12 hours before you are given Adenocor.

Pregnancy and breast-feeding
Talk to your doctor or nurse before having this medicine if:
• You are pregnant, might become pregnant, or think that you may be pregnant. You should not be given Adenocor if you are pregnant or think you may be pregnant, unless clearly necessary
• You are breast-feeding. You should not be given Adenocor if you are breast-feeding.
Ask your doctor or nurse for advice before taking any medicine if you are pregnant or breast-feeding.

If you are below 18 years of age
In children with a heart rhythm trouble called 'Wolff-Parkinson-White (WPW) syndrome', Adenocor may cause some unexpected severely abnormal heart rhythm.

Important information about some of the ingredients of Adenocor
Sodium: Adenocor contains 3.53mg sodium per dose (7.06mg/2ml vial). This should be taken into consideration by patients on a controlled sodium diet.

3. How Adenocor is given How Adenocor is given
• Adenocor is a medicine for use in hospitals
• It will be given to you by a doctor or nurse as an injection into your vein.
• Your heart and blood pressure will be closely monitored

How much Adenocor is given
If you are not sure why you are being given Adenocor or have any questions about how much Adenocor is being given to you, speak to your doctor, nurse or pharmacist.

Adults (including the elderly)
• The first dose is 3mg given over 2 seconds. This is given by rapid injection into your vein
• If the first dose does not bring your heartbeat to normal then you will be given a second dose. The second dose is 6 mg given as a rapid injection
• If the second dose does not bring your heartbeat to normal then you will be given a third dose: The third dose is 12mg given as a rapid injection
• You should not have any more doses after the 12mg dose

Infants and Children
Adenocor is a medicine for use in hospitals with resuscitation equipment available.
Your doctor will decide if this medicine is needed, how much should be given depending on your child's weight, and if several injections are needed.
• Your child will be closely monitored, including recording of his/her heart's electrical activity using an ECG (electrocardiogram) machine
• It will be given as an injection into your child vein by a doctor or nurse

If you have more Adenocor than you should
As this medicine is given to you by a doctor or nurse it is unlikely that you will be given too much. Your doctor will carefully work out how much Adenocor you should be given. As the length of time adenosine stays in the blood is very short, any side effects of too much Adenocor would quickly stop when the injection is stopped.

Sometimes you may need an injection of a medicine called aminophylline or theophylline to help with any side effects. If you have any further questions on the use of this medicine, ask your doctor, nurse or pharmacist.

4. Possible side effects

Like all medicines, Adenocor can cause side effects, although not everybody gets them. While you are being given Adenocor you may have some of the following side effects:

If any of the following side effects get worse, tell your doctor or nurse and they may stop the injection:

Side effects are generally mild, of short duration and well tolerated. However severe reactions may occur. You should tell your doctor or nurse if any of them happen.

Very common (affects more than 1 person in 10)

- Reddening of skin with a feeling of heat (flushing)
- Slow heartbeat (bradycardia)
- Skipped heart beats or extra heartbeats
- A heart problem called an AV block
- Uneven heartbeat
- Shortness of breath or the urge to breathe deeply (dyspnoea)
- Chest pressure/pain

Common (affects less than 1 person in 10)

- Feeling dizzy or light-headed
- Feeling sick (nausea)
- Headache
- Unusual skin sensations such as burning
- Feeling nervous

Uncommon (affects less than 1 person in 100)

- Blurred vision
- Fast heartbeat (tachycardia)
- Being aware of your heartbeat or feeling it 'racing'
- Metallic taste in your mouth
- Breathing more quickly or more deeply than normal (hyperventilation)
- Feeling pressure in your head, or weighed down in your arms
- Feeling of general discomfort/weakness or pain
- Sweating

Very rare (affects less than 1 person in 10 000)

- Severe breathlessness or problems in breathing
- Redness, pain or swelling at the site of injection
- Feeling uncomfortable during the injection
- Worsening of high blood pressure that affects the brain (intracranial hypertension)
- Very slow, fast or uneven heartbeats
- Severe bradycardia (very slow heartbeat)

Incidence unknown

- Allergic reactions including swelling of the face or throat, and skin reactions such as hives or rash
- Loss of consciousness, fainting
- Seizures (especially in predisposed patients)
- Vomiting

• Low blood pressure (sometimes severe)
• Severe heart problems which can be fatal (asystole, heart attack) especially in patients with underlying heart disease
• Severe breathing problems which can be fatal

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie E-mail: medsafety@hpra.ie By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Adenocor

This medicine will be kept by your doctor, nurse or pharmacist in a safe place where children cannot see or reach it. Adenocor should not be used after the expiry date which is stated on the carton and label after EXP. The expiry date refers to the last day of that month. Store below 25°C. Do not refrigerate. The product is for single use only and should be used straight away after opening. Any portion of the vial not used at once should be disposed of. Adenocor should not be used if your doctor or nurse notice any particles in the solution or any discolouration before they give you the medicine. If the appearance of the medicine has changed, the vial must be thrown away. Medicines should not be disposed of via wastewater or household waste. The pharmacist will dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Adenocor contains
• The active substance is adenosine. Each 2ml vial of Adenocor contains 6mg of adenosine (3 mg per ml).
• The other ingredients are sodium chloride and water for injections.

What Adenocor looks like and contents of the pack
Adenocor is a clear, colourless solution for injection. Each pack contains 6 vials.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder:
Sanofi-aventis Ireland Ltd. T/A SANOFI,
Citywest Business Campus, Dublin 24, Ireland. Tel: 01 4035600 Fax: 01 4035687 Email: IEmedinfo@sanofi.com

Manufacturer:
CENEXI HSC
Hérouville-Saint-Clair
2 rue Louis Pasteur,
14200 HEROUVILLE-SAINT-CLAIR
FRANCE
~~FAMAR HEALTH CARE SERVICES MADRID S.A.U.~~
~~Avenida de Leganés, 62~~
~~28923 Alcorcón (Madrid) Spain~~

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or nurse.

This leaflet was revised in ~~January 2015.~~September 2021

Adenocor® 3mg/ml solution for injection
Adenosine

1. NAME OF MEDICINAL PRODUCT
Adenocor 3mg/ml Solution for Injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each vial contains 6mg of adenosine per 2ml (3mg/ml).
Each vial also contains 0.3mmol of sodium per 2ml (0.15mmol/ml).
For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
Solution for injection. A clear, colourless solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications
Adults
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 Adenocor 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.

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

4.2 Posology and Method of Administration
Adenocor is intended for hospital use only with monitoring and cardiorespiratory resuscitation equipment available for immediate use. 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.

Adenocor 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.

Therapeutic dose
Adult:
Initial dose: 3mg given as a rapid intravenous bolus (injection 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.

Elderly
See dosage recommendations for adults.

Diagnostic dose
The above ascending dosage schedule should be employed until sufficient diagnostic information has been obtained.

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).

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 Contra-indications
Adenocor is contraindicated for patients presenting:
- Known hypersensitivity to adenosine or to any of the excipients
- Sick sinus syndrome, second or third degree Atrio-Ventricular 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
Special warnings:
Adenosine is intended for use 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. (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 or severe heart failure. Adenosine should be used with caution 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. Severe bradycardia would favour the occurrence of torsades de pointes, especially in patients with prolonged QT intervals.

The occurrence of respiratory failure (potentially fatal), asystole/cardiac arrest (potentially fatal), angina, severe bradycardia or severe hypotension should also lead to treatment discontinuation.

In patients with recent heart transplantation (less than 1 year) an increased sensitivity of the heart to adenosine has been observed.

Adenosine may precipitate or aggravate bronchospasm. See sections 4.3 and 4.8

Precautions:
Adenosine is intended for use by physicians familiar with the product (see Section 4.2 Posology and Method of Administration) 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.

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.

This medicinal product contains 0.15 mmol/ml (or 3.53 mg/ml) sodium. To be taken into consideration by patients on a controlled sodium diet.

Paediatric population
Adenosine may trigger atrial arrhythmias and thus might lead to ventricular acceleration in children with Wolff-Parkinson-White (WPW) syndrome. Also see section 5.1.

The efficacy of intraosseus administration has not been established.

4.5 Interactions with other Medicaments 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 activity. It is therefore suggested that adenosine should not be administered to patients receiving dipyrimadole; if use of adenosine is essential, dipyridamole should be stopped 24 hours beforehand, 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.

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.

Lactation: 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 applicable.

4.8 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).
Frequencies provided refer to legacy data. For newly included safety items, which are based exclusively on post-marketing experience, the frequency listed is: "Not known". The following CIOMS frequency rating is used, where applicable:
Very common: (>1/10); Common: (>1/100,<1/10) Uncommon: (>1/1000, <1/100), Rare: (>1/10000, < 1/10000, Very rare: (<1/10000), Not known (cannot be estimated from available data.).

• **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 Special Warnings and Precautions for Use)

• **Psychiatric disorders**
Common: apprehension

• **Eye disorders**
Uncommon: blurred vision

• **Vascular disorders**
Very common:
- flushing

Not known:
- hypotension sometimes severe

- cerebrovascular accident/transient ischemic attack (See section 4.4 Special Warnings and Precautions for Use)

• **Gastro-intestinal disorders**
Common: nausea

Uncommon: metallic taste

Not known: vomiting

• **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 including ventricular fibrillation and torsades de pointes (see section 4.4)

Not known:
- asystole/cardiac arrest, sometimes fatal especially in patients with underlying ischaemic heart disease/cardiac disorder (see section 4.4)
- MI/ST segment elevation especially in patients with pre-existing severe CAD (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 (see Section 4.4 Special Warnings and Precautions for Use)

Not known:
- respiratory failure (see Section 4.4 Special Warnings and Precautions for Use)
- apnoea/respiratory arrest.

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

• **Immune system disorders**
Not known:
- Anaphylactic reaction (including angioedema and skin reactions such as urticaria and rash).

• **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

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, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie E-mail: medsafety@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.
Treatment of any prolonged adverse effects should be individualised and directed towards the specific symptom.

Methylxanthines, such as caffeine, theophylline, and aminophylline are competitive antagonists of adenosine. Intravenous aminophylline or theophylline may be needed.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic Properties
Antiarrhythmic drug.

Adenosine is a purine nucleoside which is present in all cells of the body. Animal pharmacology studies in several species have shown that adenosine has a negative dromotropic effect on the atrioventricular (AV) node.

In man 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. A single 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 Adenocor can aid the diagnosis of broad or narrow complex tachycardias.

Adenocor 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 (see also section 4.4).

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.

5.2 Pharmacokinetic Properties

Adenosine is impossible to study via classical ADME protocols. 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 *in vitro* half life is estimated to be <10 seconds. The *in vivo* half life may be even shorter.

5.3 Pre-clinical 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

2 years.
Any portion of the vial not used at once should be discarded.

6.4 Special Precautions for Storage

Store below 25oC.
Do not refrigerate.

6.5 Nature and Contents of Container

Packs of six clear, Type I glass vials with chlorobutyl rubber closures secured with aluminium caps containing 2ml of solution.

6.6 Special Precautions for Disposal and other handling

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

~~7. MARKETING AUTHORISATION HOLDER~~

~~sanofi-aventis Ireland Ltd. T/A SANOFI~~
~~Citywest Business Campus~~
~~Dublin 24~~

~~8. MARKETING AUTHORISATION NUMBER~~

~~PA 540/139/1~~

~~9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION~~

~~Date of first authorisation: 16th June 1994~~
~~Date of last renewal: 16th June 2008~~

~~10. DATE OF (PARTIAL) REVISION OF TEXT~~

~~January 2015.~~