Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Amiodarone 50 mg/ml Concentrate for solution for injection/infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 50 mg of amiodarone hydrochloride
Each 3 ml ampoule contains 150 mg amiodarone hydrochloride.

Excipient with known effect: 60.6 mg of benzyl alcohol/ampoule of 3 ml sterile concentrate
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Concentrate for solution for injection/infusion (Sterile concentrate).

The product is a clear, pale yellow solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Amiodarone is indicated only for the treatment of severe rhythm disorders not responding to other therapies or when other treatments cannot be used.
Tachyarrhythmias associated with Wolff-Parkinson-White syndrome.
All types of tachyarrhythmias including supraventricular, nodal and ventricular tachycardias; atrial flutter and fibrillation; ventricular fibrillation; when other drugs have been proven ineffective or caused unacceptable side effects or when invasive anti-arrhythmic procedure is contraindicated or not effective.

4.2 Posology and method of administration

Routes of administration:
Intravenous use

Treatment should be initiated and normally monitored only under hospital or specialist supervision.
Amiodarone can be used where a rapid response is required or where oral administration is not possible.

Infusion:
The standard recommended loading dose is 5 mg/kg bodyweight in 250 ml of 5% dextrose infused within 20 minutes to 2 hours. This may be repeated 2 to 3 times during the following 24 hours (up to 1200 mg/24 hours [approximately 15 mg/kg bodyweight] in up to 500 ml 5% dextrose) and the rate of infusion is to be controlled according to the clinical response. (See section 4.4).

Injection:
In extreme clinical emergency the drug may, at the discretion of the clinician, be given as a slow injection of 150-300 mg in 10-20 ml 5% dextrose over a minimum of 3 minutes. The solution is prepared by drawing 150 mg of amiodarone = 1 ampoule to a 10 ml injection syringe and filling it up with 5% dextrose. Plain dextrose should be administered straight after the last injecting, since amiodarone is very irritating to the veins. This should not be repeated for at least 15 minutes following the first injection even though only 1 ampoule has been injected (possibility of irreversible collapse). Patients treated in this way with Amiodarone must be closely monitored, e.g., in an intensive care unit (see section 4.4).

Change over from intravenous to oral therapy:
As soon as an adequate response has been obtained, oral therapy should be initiated concomitantly at the usual loading dose (i.e. 200 mg three times a day). Amiodarone should then be phased out gradually.

Paediatric population
The safety and efficacy of amiodarone in children has not been established.
Currently available data are described in sections 5.1 and 5.2.

Due to the presence of benzyl alcohol, amiodarone intravenous administration is contraindicated in neonates, infants and children up to 3 years old.

Elderly:
As with all patients it is important that the minimum effective dose is used. Whilst there is no evidence that dosage requirements are different for this group of patients they may be more susceptible to bradycardia and conduction defects if too high a dose is employed. Particular attention should be paid to monitoring thyroid function (see sections 4.3, 4.4 and 4.8).
See section 6.2 for information on incompatibilities.

Cardiopulmonary resuscitation:
The recommended dose for ventricular fibrillations/pulse less ventricular tachycardia resistant to defibrillation is 300 mg (or 5 mg/kg body-weight) diluted in 20 ml 5% dextrose and rapidly injected followed by administration of plain dextrose after the last injection, since amiodarone is very irritating to the veins. An additional 150 mg (or 2.5 mg/kg body-weight) IV dose may be considered if ventricular fibrillation persists.

See section 6.2 for information on incompatibilities.

Hepatic and renal impairment:
Although no dosage adjustment for patients with renal or hepatic abnormalities has been defined during chronic treatment with oral amiodarone, close clinical monitoring is prudent for elderly patients e.g. in an intensive care unit.

4.3 Contraindications

- Hypersensitivity to iodine or to amiodarone hydrochloride, or to any of the excipients listed in section 6.1. (One ampoule contains approximately 56 mg iodine).
- Sinus bradycardia, sinoatrial heart block and sick sinus syndrome, unless the patient has a pacemaker (risk of sinus arrest). Atrioventricular block, bifascicular or trifascicular conduction disturbance, if the patient does not have a pacemaker.
- Evidence or history of thyroid dysfunction.
- Severe respiratory failure, circulatory collapse, or severe arterial hypotension.
- Hypotension, heart failure and cardiomyopathy are also contraindications when using Amiodarone as bolus injection.
- The combination of Amiodarone with drugs which may induce Torsades de Pointes is contra-indicated (see section 4.5).
- Due to the presence of benzyl alcohol, intravenous amiodarone is contraindicated in neonates, infants and children up to 3 years old.

The above mentioned contraindications are not relevant when amiodarone is used in the cardiopulmonary resuscitation of a patient not responding to cardiac defibrillation.

4.4 Special warnings and precautions for use

Amiodarone is only to be used when other anti-arrhythmics have shown insufficient effect.
During treatment patients must be monitored closely during treatment for adverse reactions from lungs, thyroid gland and liver.

Intravenous injection is generally not recommended due to the haemodynamic risk (severe hypotension, circulatory collapse), and intravenous infusion is to be preferred where possible. Intravenous injection must only be given in emergency situations where alternative treatment has failed, and only in a cardiac unit under continuous monitoring (ECG, blood pressure). Due to insufficient documentation, it is recommended not to use the solution for injection without prior dilution.

The dosage is about 5 mg/kg bodyweight and is given – except in case of cardiopulmonal resuscitation of shock resistant ventricular fibrillation – as an injection during at least 3 minutes. Other products must not be injected in the same IV admittance. If treatment with amiodarone hydrochloride is to be continued, it must be performed via intravenous infusion.

Paediatric patients:
Amiodarone contains benzyl alcohol (20 mg/ml). Benzyl alcohol may cause toxic reactions and allergic reactions in infants and children up to 3 years old. The neonate should be monitored closely for thyroid dysfunction.

Cardiac disorders:
Amiodarone hydrochloride has a low pro-arrhythmic effect. Onsets of new arrhythmias or worsening of treated arrhythmias, sometimes fatal, have been reported. It is important, but difficult, to differentiate a lack of efficacy of the drug from a proarrhythmic effect, whether or not this is associated with a worsening of the cardiac condition. Proarrhythmic effects generally occur in the context of drug interactions and / or electrolytic disorders (see sections 4.5. and 4.8).

Too high a dosage may lead to severe bradycardia and to conduction disturbances with the appearance of an idioventricular rhythm, particularly in elderly patients or during digitalis therapy. In these circumstances, Amiodarone treatment should be withdrawn. If necessary beta-adrenostimulants or glucagon may be given. Because of the long half-life of amiodarone hydrochloride, if bradycardia is severe and symptomatic the insertion of a pacemaker should be considered.

The pharmacological action of amiodarone hydrochloride induces ECG changes: QT prolongation (related to prolonged repolarisation) with the possible development of U-waves and deformed T-waves; these changes do not reflect toxicity.

Pulmonary disorders:
Very rare cases of interstitial pneumonitis have been reported with intravenous amiodarone hydrochloride. When the diagnosis is suspected, a chest X-ray should be performed. Amiodarone hydrochloride therapy should be re-evaluated since interstitial pneumonitis is generally reversible following early withdrawal of amiodarone hydrochloride, and corticosteroid therapy should be considered (see section 4.8).

Very rare cases of severe respiratory complications, sometimes fatal, have been observed usually in the period immediately following surgery (shock lung - adult acute respiratory distress syndrome); a possible interaction with a high oxygen concentration may be implicated (see sections 4.5 and 4.8).

Liver disorders:
Severe hepatocellular insufficiency may occur within the first 24 hours of IV amiodarone hydrochloride, and may sometimes be fatal. Close monitoring of transaminases is therefore recommended as soon as amiodarone hydrochloride is started (see section 4.8).

Endocrine disorders:
Amiodarone may induce hypothyroidism or hyperthyroidism. Monitoring of serum TSH level should be performed prior to therapy in all patients. Monitoring should be carried out regularly during treatment and for approximately 12 months following its discontinuation and when thyroid dysfunction is suspected (see section 4.8).
Amiodarone contains iodine and thus may interfere with radio-iodine uptake. However, thyroid function tests (free-T3, free-T4, usTSH) remain interpretable. Amiodarone inhibits peripheral conversion of levothyroxine (T4) to triiodothyronine (T3) and may cause isolated biochemical changes (increase in serum free-T4, free-T3 being slightly decreased or even normal) in clinically euthyroid patients. There is no reason in such cases to discontinue amiodarone treatment if there is no clinical or further biological (usTSH) evidence of thyroid disease.

Eye disorders:
If blurred or decreased vision occurs, complete ophthalmologic examination including fundoscopy should be promptly performed. Signs of optic neuropathy and/or optic neuritis should lead to the discontinuation of amiodarone due to risk of irreversible bilateral loss of vision. Ophtalmological follow-up should be performed (see section 4.8).

Caution should be exercised in patients with hypotension, decompensated cardiomyopathy and severe heart failure (also see section 4.3).

Amiodarone should only be used in a special care unit under continuous monitoring (ECG and blood pressure).

Repeated or continuous infusion via the peripheral veins may lead to injection site reactions (see section 4.8). When repeated or continuous infusion is anticipated, administration by a central venous catheter is recommended.

When given by infusion Amiodarone may reduce drop size and, if appropriate, adjustments should be made to the rate of infusion.

Anaesthesia:
Before surgery, the anaesthetist should be informed that the patient is taking amiodarone hydrochloride (see section 4.5).

Drug interactions (see section 4.5):
Concomitant use of amiodarone with the following drugs is not recommended; beta-blockers, heart rate lowering calcium channel inhibitors (verapamil, diltiazem) which may cause hypokalaemia.
In patients taking amiodarone concomitantly with simvastatin, the dose of simvastatin should not exceed 20 mg/day.

4.5 Interaction with other medicinal products and other forms of interaction

In view of the long and variable half-life of amiodarone (approximately 50 days), potential for drug interactions exists not only with concomitant medication but also with drugs administered after discontinuation of amiodarone.

Combinations that are contraindicated:
Combined therapy with the following drugs which prolong the QT interval is contra-indicated (see section 4.3) due to the increased risk of Torsades de Pointes; for example:
- Class Ia anti-arrhythmic drugs e.g. quinidine, procainamide, disopyramide.
- Class III anti-arrhythmic drugs e.g. sotalol, bretylium.
- Intravenous erythromycin, co-trimoxazole or pentamidine injection.
- Some anti-psychotics e.g. chlorpromazine, thioridazine, fluphenazine, pimozide, haloperidol, amisulpiride and sertindole.
- Lithium and tricyclic anti-depressants e.g. doxepin, maprotiline, amitriptyline.
- Certain antihistamines e.g. terfenadine, astemizole, mizolastine.
- Anti-malarials e.g. quinine, mefloquine, chloroquine, halofantrine.

Combinations that are not recommended:
Combined therapy with the following drugs is not recommended:
- Beta blockers and certain calcium channel inhibitors (diltiazem, verapamil); potentiation of negative chronotropic properties and conduction slowing effects may occur.
- Stimulant laxatives, which may cause hypokalaemia thus increasing the risk of Torsades de Pointes; other types of laxatives should be used.

Caution is advised:
Caution should be exercised over combined therapy with the following drugs which may cause hypokalaemia and/or hypomagnesaemia, e.g. diuretics, systemic corticosteroids, tetracosactrin, intravenous amphotericin.

In cases of hypokalaemia, corrective action should be taken and QT interval monitored. In case of Torsades de Pointes,

antiarrhythmic agents should not be given; pacing may be instituted and IV magnesium may be used.

*Oral anticoagulants**:***
Amiodarone hydrochloride raises the plasma concentrations of oral anticoagulants (warfarin) by inhibition of CYP 2C9. The dose of warfarin should be reduced accordingly. More frequent monitoring of prothrombin time both during and after amiodarone hydrochloride treatment is recommended.

Digoxin:
Administration of Amiodarone to a patient already receiving digoxin will cause an increase in the plasma digoxin concentration and thus precipitate symptoms and signs associated with high digoxin levels. Clinical, ECG, and biological monitoring are recommended and digoxin dosage usually has to be reduced. A synergistic effect on heart rate and atrioventricular conduction is also possible.

Phenytoin:
Amiodarone hydrochloride raises the plasma concentrations phenytoin by inhibition of CYP 2C9. Phenytoin dosage should be reduced if signs of overdosage appear, and plasma levels may be measured**.**

Flecainide:
Possible increase of flecainide plasma levels; dosage of flecainide by inhibition of CYP 2D6; the dosage of flecainide should be adjusted.

Drugs metabolised by cytochrome P450 3A4:
When such drugs are co-administered with amiodarone hydrochloride, an inhibitor of CYP 3A4, this may result in a higher level of their plasma concentrations, which may lead to a possible increase in their toxicity.

Cyclosporin:
Combination with amiodarone hydrochloride may increase cyclosporin plasma levels. Dosage should be adjusted.

Fentanyl:
Combination with amiodarone hydrochloride may enhance the pharmacologic effects of fentanyl and increase the risk of its toxicity.

Other drugs metabolised by CYP 3A4:
Lidocaine, tacrolimus, sildenafil, ergotamine; simvastatin and other statins metabolised by CYP 3A4 (increased risk of muscular toxicity).

Interaction with substrates of other CYP 450 isoenzymes:
In vitro studies show that amiodarone also has the potential to inhibit CYP 1A2, CYP 2C19 and CYP 2D6 through its main metabolite. When co-administered, amiodarone would be expected to increase the plasma concentration of drugs whose metabolism is dependent upon CYP 1A2, CYP 2C19 and CYP 2D6.

Grape fruit juice:
Grapefruit juice inhibits cytochrome P450 3A4 and may increase the plasma concentration of amiodarone hydrochloride. Grapefruit juice should be avoided during treatment with amiodarone hydrochloride.

General anaesthesia:
Caution is advised in patients undergoing general anaesthesia, or receiving high dose oxygen therapy. There is some evidence that the presence of amiodarone possibly increases the risk of complications (atropine-resistant bradycardia, hypotension, decreased cardiac output) during general anaesthesia. A few cases of adult respiratory distress syndrome most often in the period immediately after surgery have been observed. A possible interaction with a high oxygen concentration may be implicated.

4.6 Fertility, pregnancy and lactation

Pregnancy:
There is only insufficient experience on the safety of administration during pregnancy.

In view of the effect of amiodarone hydrochloride on the foetal thyroid gland, amiodarone hydrochloride should not be used during pregnancy unless clearly necessary. The product can be used in pregnant at life-threatening and pregnancy threatening arrhythmias.

Lactation:
Amiodarone hydrochloride is excreted in the breast milk in significant quantities. If therapy is required during the lactation period, or if amiodarone hydrochloride was taken during pregnancy, breast-feeding should be stopped.

4.7 Effects on ability to drive and use machines

Some of the undesirable effects mentioned in section 4.8 may impair ability to drive and use machines. However this section is not relevant as
Amiodarone is only given in a hospital or emergency medicine surroundings.

4.8 Undesirable effects

Frequency **System Organ Class**	**Common** (≥1/100, <1/10)	**Rare** (≥1/10,000 <1/1,000)	**Very Rare** (<1/10,000)**, Not known** (*cannot be estimated from the available data*)
Immune system disorders:		The excipient benzyl alcohol may cause hypersensitivity reactions.	Anaphylactic shock.
Endocrine disorders:			Hypothyroidism including myxoedema coma, Hyperthyroidism including thyrotoxicosis, Syndrome of inappropriate antidiuretic hormone secretion (SIADH)
Psychiatric disorders:			Delirium (including confusion)
Nervous system disorder:			Benign intra-cranial hypertension (pseudo tumour cerebri), headache.
Eye disorders			Optic neuropathy/neuritis (see section 4.4).
Cardiac disorder:	Bradycardia, generally moderate.		Marked bradycaria, sinus arrest requiring discontinuation of amiodarone hydrochloride, especially in patients with sinus node dysfunction and/or in elderly patients. Onset or worsening of arrhythmia, sometimes

			followed by cardiac arrest.
Vascular disorders:	Decrease in blood pressure, usually moderate and transient. Cases of severe hypotension or collapse have been reported following overdosage or a too rapid injection.		
Respiratory, thoracic and mediastinal disorder:			Interstitial pneumonitis. Severe respiratory complications (adult acute respiratory distress syndrome), sometimes fatal. Bronchospasm and/or apnoea in case of severe respiratory failure, especially in asthmatic patients.
Gastrointestinal disorder:			Nausea, Pancreatitis (acute).
Hepatobiliary disorder:			Isolated increase in serum transaminases, which is usually moderate (1.5 to 3 times normal range) at the beginning of therapy. They may return to normal with dose reduction or even spontaneously. Acute liver disorders with high serum transaminases and/or jaundice, including hepatic failure, sometimes fatal.
Skin and subcutaneous tissue disorders:	Eczema		Sweating, Severe skin reaction as toxic epidermal necrolysis (TEN)/Stevens-Johnson syndrome (SJS), bullous dermatitis and Drug reaction with eosinophilia and systematic

			symptoms (DRESS)
Musculoskeletal and Connective Tissue Disorders			Back pain
General disorders and administration site conditions:	Injection site reactions such as pain, erythema, oedema, necrosis, extravasation, infiltration, inflammation, induration, thrombophlebitis, phlebitis, cellulitis, infection, pigmentation changes.		

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

Some information regarding acute overdosage with amiodarone hydrochloride is available. Few cases of sinus bradycardia, heart block, attacks of ventricular tachycardia, Torsades de Pointes, circulatory failure and hepatic injury have been reported.

Symptoms:
Dizziness, headache, AV block, bradycardia, arrhythmias, heart failure, fall in blood pressure, nausea, vomiting (see also section 4.8).

Treatment:
In the event of overdose treatment should be symptomatic, in addition to general supportive measures. The patient should be monitored and if bradycardia occurs, beta-adrenostimulants or glucagon may be given. Spontaneously resolving attacks of ventricular tachycardia may also occur. Due to the pharmacokinetics of amiodarone hydrochloride, adequate and prolonged surveillance of the patient, particularly cardiac status, is recommended.

In case of suspected overdose, the infusion must be stopped immediately.

Neither amiodarone hydrochloride nor its metabolites are dialysable.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antiarrythmic (Class III), ATC code: C01B D01

Amiodarone is a di-iodinated benzofuran derivative and is classified as a class III antiarrhythmic agent owing to its ability to increase the cardiac action potential duration in both atrial and ventricular myocytes via block of cardiac K+ channels (mainly of both the rapid and slow components of the delayed rectifier K+ current, IKr and IKs, respectively). Thus, it prolongs the refractory period of the action potential leading to depression of ectopies and re-entry-arrhythmias

and to prolongation of the QTc interval in the ECG. Furthermore, amiodarone also blocks cardiac Na+ currents (class I effect) and Ca2+ currents (class IV effect). The latter may lead to slowing of conduction through the sinoatrial and atrioventricular nodes. During long-term administration, amiodarone also seems to inhibit the trafficking of ion channels from the endoplasmic reticulum to the plasma membrane in cardiac myocytes, and these effects may contribute to cardiac electrophysiological actions of amiodarone under chronic administration.

Furthermore, amiodarone is a non-competitive antagonist at both ß- and α-adrenoceptors and, therefore, has haemodynamic effects: dilatation of coronary arteries and peripheral vasodilation leading to a reduction of systemic blood pressure. Negative inotropic, negative chronotropic and negative dromotropic effects seem to be induced by the ß-adrenergic antagonistic effects induced by amiodarone. Amiodarone is a potent inhibitor of iodothyronine-5´-monodeiodinase activity (the main T4-T3 converting enzyme). Some effects of amiodarone are comparable with hypothyroidism, which might be due to inhibition of thyroid hormone synthesis. In rats, increases in serum thyroid-stimulating hormone (TSH), thyroxine (T4) and reverse triiodothyronine (rT3), and decreases in serum triiodothyronine (T3) as a result of deiodination of T4 to T3 have been observed. These antithyroid actions of amiodarone might contribute to its cardiac electrophysiological effects. The main metabolite desethylamiodarone has effects on cardiac electrophysiology similar to those of the parent compound.

Paediatric population:
No controlled paediatric studies have been undertaken.

In published studies the safety of amiodarone was evaluated in 1118 paediatric patients with various arrhythmias. The following doses were used in paediatric clinical trials.

Oral
- Loading dose: 10 to 20 mg/kg/day for 7 to 10 days (or 500 mg/m/day if expressed per square meter).
- Maintenance dose: the minimum effective dosage should be used; according to individual response, it may range between 5 to 10 mg/kg/day (or 250 mg/m/day if expressed per square meter).

Intravenous
- Loading dose: 5 mg/kg body weight over 20 minutes to 2 hours.
- Maintenance dose: 10 to 15 mg/kg/day from few hours to several days.

If needed oral therapy may be initiated concomitantly at the usual loading dose.

5.2 Pharmacokinetic properties

Pharmacokinetics of amiodarone hydrochloride is unusual and complex, and has not been completely elucidated. Absorption following oral administration is variable and may be prolonged, with enterohepatic cycling. The major metabolite is desethylamiodarone. Amiodarone hydrochloride is highly protein bound > 95%). Renal excretion is minimal and faecal excretion is the major route. A study in both healthy volunteers and patients after intravenous administration of amiodarone hydrochloride reported that the calculated volumes of distribution and total blood clearance using a two-compartment open model were similar for both groups. Elimination of amiodarone hydrochloride after intravenous injection appeared to be biexponential with a distribution phase lasting about 4 hours. The very high volume of distribution combined with a relatively low apparent volume for the central compartment suggests extensive tissue distribution. A bolus iv injection of 400 mg gave a terminal $T_{½}$ of approx 11 hours.

Paediatric population:
No controlled paediatric studies have been undertaken. In the limited published data available in paediatric patients, there were no differences noted compared to adults.

5.3 Preclinical safety data

In chronic toxicity studies, amiodarone led to pulmonary damage (fibrosis, phospholipidosis; in hamsters, rats and dogs) as well as CNS disorders (in rats). Pulmonary damage appears to be predominantly caused by oxidative stress and free radicals. In addition, amiodarone caused liver damage in rats. The action of amiodarone on serum lipids may indirectly result from altered plasma concentrations of thyroid gland hormones.

Amiodarone is a marked phototoxic substance. There is evidence that UV radiation can cause cytotoxically acting free radicals in the presence of amiodarone. This may not only lead to acute phototoxic reactions, but also to damage of the DNA (photomutagenicity) and subsequent photocancerogenic actions. Up to now these potentially severe side effects of amiodarone have not been investigated experimentally. Thus the photomutagenic and the photocancerogenic potential of amiodarone are not known. In a 2-years carcinogenicity study in rats, amiodarone caused an increase in thyroid follicular tumours (adenomas and/or carcinomas) in both sexes at clinical relevant exposures. Since mutagenicity findings were negative, an epigenic rather than genotoxic mechanism is proposed for this type of tumour induction. In the mouse, carcinomas were not observed, but a dose-dependent thyroid follicular hyperplasia was seen. These effects on the thyroid in rats and mice are most likely due to effects of amiodarone on the synthesis and/or release of thyroid gland hormones. The relevance of these findings to man is low.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl alcohol
Polysorbate 80
Water for injections
Hydrochloric acid (pH adjustment)
Sodium hydroxide (pH adjustment)

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

Amiodarone is incompatible with saline solution and should be administered solely in 5% dextrose solution. Solutions containing less than 300 mg (two ampoules) Amiodarone in 500 ml dextrose 5% are unstable and should not be used.

The following active substances or solution for reconstitution/dilution or equipment/devices should not be administered simultaneously:
The use of administration equipment or devices containing plasticizers such as DEHP (di-2-ethylhexylphthalate) in the presence of amiodarone hydrochloride may result in leaching out of DEHP. In order to minimise patients' exposure to DEHP, the final amiodarone hydrochloride dilution for infusion should preferably be administered through non DEHP-containing sets.

6.3 Shelf life

2 years.
Reconstituted/diluted solution: After dilution in dextrose 5 %, chemical and physical in-use stability has been demonstrated for 36 hours at 25 °C when exposed to light.
From a microbiological point of view, the diluted solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 °C to 8 °C unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store in a refrigerator (2°C to 8°C).
Store in the original package in order to protect from light.
For storage conditions of the reconstituted/diluted product see section 6.3.

6.5 Nature and contents of container

Clear, type I glass ampoules containing 3 ml solution.
Pack size: 5 x 1 ampoule, 10 x 1 ampoule.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

For single use only. Discard any unused solution.
The dilution is to be made under aseptic conditions. The solution is to be inspected visually for particulate matter and discoloration prior to administration. The solution should only be used if the solution is clear and free from particles.

Solutions containing less than 300 mg of amiodarone (two ampoules) in 500 ml of dextrose are not stable and must not be used. It should also be stressed that no other compounds are to be mixed with amiodarone infusion solution.

Amiodarone should be administered solely in 5% dextrose solution.
Amiodarone must not be mixed with other medicinal products in the same syringe.

Intravenous infusion:
The calculated dose is diluted with 250 ml 5% dextrose. See section 4.2.

Intravenous injection:
150-300 mg (corresponding to 3-6 ml Amiodarone) is diluted with 10-20 ml 5% dextrose. See section 4.2.

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

7 MARKETING AUTHORISATION HOLDER

Stragen UK Ltd
Castele Court
41 London Road
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UK

8 MARKETING AUTHORISATION NUMBER

PA1294/005/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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