PACKAGE LEAFLET: INFORMATION FOR THE USER

Amiodarone 150mg/3ml Concentrate for Solution for Injection/Infusion

Amiodarone hydrochloride

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again
- If you have any further questions, ask your doctor, pharmacist or nurse
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Amiodarone is and what it is used for

Amiodarone 150mg/3ml Concentrate for Solution for Injection/Infusion (called Amiodarone in this leaflet) contains a medicine called amiodarone hydrochloride. This belongs to a group of medicines called anti-arrhythmics.

It works by controlling the uneven beating of your heart (called 'arrhythmias'). Having the injection helps your heartbeat to return to normal.

Amiodarone is normally only given in a hospital when a quick response is needed or when tablets cannot be given.

Amiodarone can be used to:

- Treat uneven heartbeats where other medicines either have not worked or cannot be used
- Treat an illness called Wolff-Parkinson-White Syndrome. This is where your heart beats unusually fast
- Treat other types of fast or uneven heartbeats known as 'atrial flutter' or 'atrial fibrillation'. Amiodarone is used only when other medicines cannot be used
- Treat fast heartbeats which may happen suddenly and may be uneven. Amiodarone is used only when other medicines cannot be used

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

Do not use this medicine and tell your doctor, pharmacist or nurse if you:

- are allergic to iodine, amiodarone, or any of the other ingredients of Amiodarone (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
- have a slower than usual heartbeat (called 'sinus bradycardia') or an illness called 'sino-atrial' heart block
- have any other problems with your heartbeat and do not have a pacemaker fitted
- have or have previously had thyroid problems. Your doctor should test your thyroid before giving you this medicine
- have severe breathing problems
- have serious blood circulation problems
- have very low blood pressure

- are taking certain other medicines which could affect your heartbeat (see 'Other medicines and Amiodarone' below)
- are pregnant or breast-feeding (see 'Pregnancy and breast-feeding' below)

This product must not be given to children, premature babies or neonates.

Do not use this medicine if any of the above apply to you. If you are not sure, talk to your doctor, pharmacist or nurse before using Amiodarone.

If you are on a heart transplant waiting list, your doctor may change your treatment. This is because taking Amiodarone before heart transplantation has shown an increased risk of a life-threatening complication (primary graft dysfunction) in which the transplanted heart stops working properly within the first 24 hours after surgery.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before you are given Amiodarone.
Amiodarone should be given with care if you:
- have a weak heart ('cardiomyopathy') or heart failure
- have low blood pressure
- have any problems with your lungs including asthma
- have a problem with your thyroid gland
- are about to have an operation
- are an elderly person (> 60 years)
- have liver problems
- require oxygen treatment
- are to undergo a general anaesthetic
- have any problems with your eyesight. This includes an illness called 'optic neuritis' or 'neuritis'
- are taking certain other medicines – for list of medicines see section "Other medicines and Amiodarone" below
- have blistering or bleeding of the skin, including around your lips, eyes, mouth, nose and genitals. You may also have flu-like symptoms and fever. This may be something called 'Stevens-Johnson syndrome'
- have a severe blistering rash in which layers of the skin may peel off to leave large areas of raw exposed skin over the body. You may also feel generally unwell, have a fever, chills and aching muscles (Toxic Epidermal Necrolysis)
- currently take a medicine containing sofosbuvir for the treatment of hepatitis C as it may result in a life-threatening slowing of your heartbeat. Your doctor may consider alternative treatments. If treatment with amiodarone and sofosbuvir is needed, you may require additional heart monitoring.

Tell your doctor immediately if you are taking a medicine containing sofosbuvir for the treatment of hepatitis C and during treatment you experience:
- Slow or irregular heartbeat or heart rhythm problems
- Shortness of breath or worsening of existing shortness of breath
- Chest pain
- Light-headedness
- Palpitations
- Near-fainting or fainting

If you are not sure if any of the above apply to you, talk to your doctor, nurse or pharmacist before having Amiodarone.

Children
This medicine should not be given to neonates, infants and children up to 3 years old.

Other medicines and Amiodarone
Tell your doctor, pharmacist or nurse if you are taking or have recently taken or might take any other medicines. This includes medicines you buy without a prescription, including herbal medicines. This is because Amiodarone can affect the way some other medicines work. Also, some medicines can affect the way Amiodarone works.

In particular, do not take this medicine and tell your doctor, if you are taking:
- medicines which may cause heart rhythm disturbance (called torsades de pointes)
- other medicines to treat irregular heartbeat (such as quinidine, procainamide, disopyramide, sotalol or bretylium)
- some antibiotics (such as erythromycin injection, co-trimoxazole, moxifloxacin or pentamidine injection)
- medicines for schizophrenia (such as chlorpromazine, thioridazine, fluphenazine, pimozide, haloperidol, amisulpride or sertindole)
- medicines for other mental illnesses (such as lithium, doxepin, maprotiline or amitriptyline)
- medicines for malaria (such as quinine, mefloquine, chloroquine or halofantrine)
- medicines used for hay fever, rashes or other allergies called antihistamines (such as terfenadine, astemizole or mizolastine)
- sofosbuvir, used for the treatment of hepatitis C
- gastrointestinal agents e.g. cisapride, droperidol
- Amiodarone tablets

Tell your doctor if you are taking any of the following medicines:
- medicines for infection (such as ciprofloxacin, ofloxacin or levofloxacin)
- medicines for heart problems called beta-blockers (such as propranolol)
- medicines called calcium channel blockers for chest pain (angina) or high blood pressure (such as diltiazem or verapamil)
- medicines for constipation (laxatives) such as bisacodyl or senna
- medicines for high cholesterol (statins) such as simvastatin or atorvastatin

The following medicines can increase the chance of you getting side effects, when taken with Amiodarone:
- Amphotericin (when given directly into a vein) used for fungal infections
- Corticosteroids used for inflammation such as hydrocortisone, betamethasone or prednisolone
- Water tablets (diuretics) such as furosemide
- General anaesthetics or high dose oxygen – used during surgery
- Tetracosactide - used to test some hormone problems
- Amiodarone tablets - used to control the uneven beating of the heart called ‘arrhythmias’

Amiodarone may increase the effect of the following medicines:
- Tetracosactrin (used in some blood tests or sometimes in the treatment of Crohn's disease)
- Drugs which may change the levels of potassium or magnesium in your blood e.g. diuretics (water tablets), steroid tablets
- Monoamine oxidase inhibitors (medications used in high blood pressure)
- Warfarin – used for thinning the blood. Your doctor should reduce your dose of warfarin and monitor your treatment closely
- Digoxin – used for heart problems. Your doctor should monitor your treatment closely and may halve your dose of digoxin
- Phenytoin – used to treat fits
- Flecainide - another medicine used for uneven heartbeats. Your doctor should monitor your treatment closely and may halve your dose of flecainide
- Ciclosporin, tacrolimus and sirolimus - used to help prevent rejection of transplants
- Medicines for impotence such as sildenafil, tadalafil or vardenafil
- Fentanyl - used for pain relief
- Ergotamine - used for migraines

- Midazolam - used to treat anxiety or to help you relax before surgery
- Lidocaine – used as an anaesthetic

If you are not sure if any of the above apply to you, talk to your doctor, nurse or pharmacist before taking Amiodarone.

Amiodarone with food and drink
Do not drink grapefruit juice while taking this medicine. This is because drinking grapefruit juice while taking Amiodarone can increase your chance of getting side effects.
You should limit the amount of alcohol you drink whilst being treated with this medicine.

Protect your skin from sunlight
Keep out of direct sunlight while taking this medicine and for a few months after you have finished taking it. This is because your skin will become much more sensitive to the sun and may burn, tingle or severely blister if you do not take the following precautions:
- make sure you use high factor sun cream
- always wear a hat and clothes which cover your arms and legs.

Pregnancy and breast-feeding
Do not take this medicine if
- you are pregnant, might become pregnant or think you may be pregnant
- you are breast-feeding or planning to breast feed.

Ask your doctor or pharmacist for advice before taking any medicine if you are pregnant or breast-feeding. Your doctor will prescribe Amiodarone only if he/she considers the benefit of treatment outweighs the risks during your pregnancy. Amiodarone can be used during pregnancy in life-threatening circumstances only.

Driving and using machines
Your doctor will tell you how long to wait before driving a car or using machines after you are given this medicine.

Amiodarone Injection contains:
- Iodine: Amiodarone Injection contains about 56 mg of iodine in one ampoule of 3 ml. Iodine is present in amiodarone hydrochloride, the medicine your infusion contains. Iodine can cause problems to your thyroid (see 'Tests' below)
- Benzyl Alcohol: Amiodarone Injection contains 60 mg benzyl alcohol in each 3 ml ampoule which is equivalent to 20 mg/ml. Benzyl alcohol may cause allergic reactions. Benzyl alcohol has been linked with the risk of severe side effects including breathing problems (called "gasping syndrome") in young children. This medicine should not be given to neonates, infants and children up to 3 years old. Ask your doctor or pharmacist for advice if you are pregnant, breast-feeding or you have liver or kidney disease. This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called "metabolic acidosis").

3. How you will be given Amiodarone

Your doctor or nurse will normally give you Amiodarone. This is because it needs to be given as an infusion into your vein in the hospital where the doctor can monitor your progress.

Using this medicine
- This medicine will be diluted before it is given to you
- Your doctor will change you over to Amiodarone tablets as soon as possible
- If you feel the effect of your medicine is too weak or too strong, tell your doctor, nurse or pharmacist

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

How much will be given to you
Your doctor will decide how much to give you depending on your illness.

Adults (including elderly)

Starting dose
The standard recommended dose is 5mg/kg bodyweight. However, this may vary depending upon your age and how well you respond to treatment. This medicine will be diluted using 5% glucose solution before it is given to you over a period of 20 minutes to 2 hours. It will be given slowly, usually via a drip into a vein in your arm or chest. Depending on your response, you may be given further infusions up to 1200mg (approximately 15mg/kg bodyweight) in up to 500ml 5% glucose per 24 hours.

Maintenance dose
10 - 20mg per kg bodyweight in physiological glucose solution can be given every 24 hours (on average 600 to 800mg/ 24 hours up to a maximum of 1200mg/ 24 hours, equivalent to 4-5 ampoules, maximum 8 ampoules) for a few days. In some conditions the medicine may be given as a slow injection of 150-300mg in 10-20ml 5% glucose over a minimum of 3 minutes. If Amiodarone is given in this way you will be closely monitored. As soon as an adequate response has been obtained using intravenous treatment, you may be switched to oral treatment.
Elderly patients should be closely monitored during treatment, particularly for thyroid function.

Use in children and adolescents
There are only limited data on the efficacy and safety in children. Your doctor will decide on an appropriate dose.

Patients with liver and kidney problems
Although no dosage adjustment for patients with kidney or liver abnormalities has been defined during chronic treatment with oral amiodarone, close clinical monitoring is prudent for elderly patients.

If you have any further questions on the use of this product, ask your doctor or the other healthcare professionals.

If you use more Amiodarone than you should
Your doctor will carefully calculate how much Amiodarone you should get. Therefore, it is unlikely your doctor, nurse or pharmacist will give you too much of this medicine. But, if you think that you have been given too much or too little Amiodarone, tell your doctor, nurse or pharmacist.

The following effects may happen: feeling dizzy, faint, sick, tired or confused; having an abnormally slow or fast heartbeat. Too much amiodarone can damage the heart and liver.

If you forget to use Amiodarone
Your doctor or nurse will have instructions on when to give you this medicine. It is unlikely that you will not be given the medicine as it has been prescribed. However, if you think you may have missed a dose, then talk to your doctor or nurse.

If you stop using Amiodarone
It is important for you to keep having Amiodarone injections until your doctor decides to stop them. If you stop having this medicine the uneven heartbeats may come back. This could be dangerous.

Tests

Your doctor will do regular tests to check how your liver is working. Amiodarone can affect how your liver works. If this happens, your doctor will decide whether you should keep having this medicine. Your doctor may do regular thyroid tests while you are taking this medicine. This is because Amiodarone contains iodine which can cause problems to your thyroid.

Your doctor may also do other regular tests such as blood tests, chest X-rays, ECG (electrical test of your heartbeat) and eye tests both before and while you are having Amiodarone.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Amiodarone may stay in your blood for up to a month after stopping treatment.
You may still get side effects in this time.

If any of the following happen, tell your doctor immediately. These are very serious side effects and you may need urgent medical attention.

- you have a severe allergic reaction - you may experience a sudden itchy rash (hives), swelling of the hands, feet, ankles, face, lips, mouth or throat (which may cause difficulty in swallowing or breathing), you may feel you are going to faint and there may be inflammation of some of your blood vessels
- your heartbeat becomes very slow or stops beating. You may also feel dizzy, unusually tired and short of breath. This may occur especially in people over 65 years old or to people with other heartbeat problems
- your heartbeat becomes even more uneven or erratic. This can lead to a heart attack, so you should go to hospital straight away
- you get yellowing of the skin or eyes (jaundice), feel tired or sick, loss of appetite, stomach pain or high temperature. These can be signs of liver problems or damage which can be very dangerous
- you have difficulty breathing or tightness in the chest, coughing which will not go away, wheezing, weight loss and fever. This could be due to inflammation of your lungs which can be very dangerous
- you have a life-threatening irregular heart beat (*Torsade de pointes*)
- you experience blistering or peeling of the skin around the lips, eyes, mouth, nose and genitals, flu-like symptoms and fever. This could be a condition called *Stevens-Johnson syndrome*
- you have a severe blistering rash in which layers of the skin may peel off to leave large areas of raw exposed skin over the body. You may also feel generally unwell, have a fever, chills and aching muscles (*Toxic Epidermal Necrolysis*)
- you have inflamed skin characterised by fluid filled blisters (*bullous dermatitis*)
- you have flu like symptoms and a rash on the face followed by an extended rash with a high temperature, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophil) and enlarged lymph nodes (*DRESS*)
- Headache (which is usually worse in the morning or happens after coughing or straining), feeling sick (nausea), fits, fainting, eyesight problems or confusion can occur. These could be signs of problems with your brain

If you experience any of the following tell your doctor as soon as possible.

Very common (may affect more than 1 in 10 people)

- blurred eyesight or seeing a coloured halo in dazzling light
- burning more easily in the sun (see ‘Protect your skin from sunlight’ in Section 2)

Common (may affect up to 1 in 10 people)

- itchy, red rash (eczema)
- generally moderate slow heart rate
- decrease in blood pressure
- local injection site reactions including swelling, pain, redness, infection, and pigmentation changes (blue or grey marks on parts of your skin exposed to sunlight, especially the face)
- feeling extremely restless or agitated, weight loss, increased sweating and being unable to stand the heat. These could be signs of an illness called 'hyper-thyroidism'
- feeling extremely tired, weak or run-down, weight gain, being unable to stand the cold, constipation and aching muscles. These could be signs of an illness called hypo-thyroidism
- trembling when you move your arms or legs
- muscle weakness
- nightmares
- problems sleeping
- dizziness, lightheadedness, fainting. This may occur temporarily and is due to lowering of blood pressure
- decrease in sex drive.

Uncommon (may affect up to 1 in 100 people)
- feeling numb or weak, tingling or burning feelings in any part of your body
- dizziness

Rare (may affect up to 1 in 1,000 people)
- the excipient benzyl alcohol may cause hypersensitivity reactions

Very rare (may affect up to 1 in 10,000 people)
- chest pain or palpitations, or abnormal heart rhythm
- nausea
- liver disorders
- inability to breathe
- hot flushes
- sweating
- red, scaly patches of skin, loss of hair or loosening of nails (called 'exfoliative dermatitis')
- loss of eyesight in one eye or your eyesight becomes dim and colourless. Your eyes may feel sore or tender and feel painful to move. This could be an illness called 'optic neuropathy or neuritis'
- skin rash
- skin redness during radio-therapy
- moving unsteadily or staggering, slurred or slow speech
- headache (which is usually worse in the morning or happens after coughing or straining), feeling sick (nausea), fits, fainting, eyesight problems or confusion can occur. These could be signs of problems with your brain
- balance problems, feeling dizzy (vertigo)
- headache
- feeling unwell, confused or weak, feeling sick (nausea), loss of appetite, feeling irritable. This could be an illness called 'syndrome of inappropriate anti-diuretic hormone secretion' (SIADH)
- changes in the amount of liver enzymes at the beginning of treatment.

Not known (frequency cannot be estimated from the available data)
- seeing, hearing or feeling things that are not there (hallucinations)
- sudden inflammation of the pancreas which causes severe pain in the abdomen and back (pancreatitis)
- confusion (delirium)
- hives (itchy, lumpy rash)
- back pain
- decreased sex drive

- life-threatening complication after heart transplantation (primary graft dysfunction) in which the transplanted heart stops working properly (See section 2)
- you may get more infections than usual. This could be caused by a decrease in the number of white blood cells (neutropenia)
- severe reduction in the number of white blood cells which makes infections more likely (agranulocytosis).

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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Amiodarone

This medicine will be kept by your doctor or pharmacist in a safe place where children cannot see or reach it.
Do not use Amiodarone 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.
Do not store above 25°C. Do not refrigerate or freeze.
Storage at low temperature could cause the formation of precipitate. Store in the original container.
Do not use unless solution is clear. Only clear solutions free of particles should be used. Reject any portion not used immediately after the opening of the ampoule. After dilution, use the solution immediately and reject any portion unused.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What Amiodarone contains
The active substance is amiodarone hydrochloride.
The other ingredients are Polysorbate 80, Benzyl alcohol, Hydrochloride acid or Sodium Hydroxide, Water for injection.

What Amiodarone looks like and contents of the pack
Amiodarone is a pale yellow solution and is available as 3ml glass ampoules in cartons of 5 or 10 units.

Marketing Authorisation Holder:
Ibigen S.r.l. - Via Fossignano, 2, 04011 Aprilia (LT) – Italy

Manufacturer:
Bioindustria Laboratorio Medicinali S.p.A.
Via De Ambrosiis, 2, 15067 Novi Ligure (AL) – Italy

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The following information is intended for healthcare professionals only

For single dose use only. Discard any unused solution immediately after initial use.
Any unused product or waste material should be disposed of in accordance with local requirements.
The dilution is to be made under aseptic conditions. Before use, the sterile concentrate should be visually inspected for clarity, particulate matter, discolouration and the integrity of the container. The

solution should only be used if it is clear, free from particles and the container is undamaged and intact.

Amiodarone should be administered by a central venous route, except for cardiopulmonary resuscitation in case of cardiac arrest related to ventricular fibrillation resistant to defibrillation, where the peripheral venous route could be used.

Cardiopulmonary resuscitation
Administration by a central venous catheter is recommended when it is immediately available, if not, the administration must be done by a peripheral venous route, using a large peripheral vein and with a flow as important as possible, or possibly, by a slow injection over a minimum of 3 minutes, followed by administration of 200ml of infusion fluid. Do not give other medicinal substances in the same syringe with amiodarone. Amiodarone can cause severe irritation of the vein, therefore adequate rinsing after bolus injection must be ensured. In treatment of prolonged, refractory ventricular fibrillation, after administration of adrenaline and defibrillation, administer 300mg as bolus injection and repeat, if necessary, with 150mg bolus injection.