venous catheter should be considered. Some intravenous preparations of amiodarone contain benzyl alcohol, a preservative that has caused fatal 'gasping syndrome' in neonates (see Neonates, under Benzyl Alcohol,), and should be avoided in infants and children up to 3 years old.
Some of the contra-indications for amiodarone may not apply when it is given intravenously in emergency situations.

PREGNANCY

Each 200-mg tablet of amiodarone contains about 75 mg of iodine. The potential effect of this iodine load on the foetus has limited the use of amiodarone in pregnancy since iodine freely crosses the placenta and may cause thyroid disorders in the fetus. In addition, amiodarone and desethyl-amiodarone both cross the placenta, with respective concentrations in cord blood at delivery of about 10 % and 25 % of the maternal plasma concentrations, and direct effects on the fetus are therefore possible. However, a review of 64 reported cases of arniodarone use during pregnancy found no evidence of an increased incidence of fetal malformations; hypothyroidism occurred in 14 neonates (22 %) , but only 2 had detectable goitre, and neonates had transient hyperthyroidism. Neurodevelopmental follow-up was limited, but mild abnormalities were reported in some cases; this appeared to be independent of thyroid status, suggesting it may have been due to a direct effect of amiodarone. In view of its effects on the fetal thyroid gland, amiodarone is contraindicated during pregnancy, except if the benefits outweigh the risks.

BREAST FEEDING.

Amiodarone is distributed into breast milk and significant amounts may be ingested if infants are breast fed. Licensed product information therefore contra-indicates the use of amiodarone during breast feeding, and the American Academy of Pediatrics considers that the use of amiodarone may be of concern due to the risk of hypothyroidism in the infant. In one study, amiodarone was still detectable in breast milk several weeks after amiodarone was stopped, suggesting that caution is still required. However, there has been a report of an infant who was successfully breast fed with close monitoring of thyroid function; the mother stopped amiodarone at delivery.

ADVERSE EFFECTS:

Adverse effects are common with amiodarone. Many are dose-related and reversible with reduction in dose; however, because of its long half-life this can take some time and adverse effects may develop after treatment is stopped.
Adverse cardiovascular effects associated with amiodarone include severe bradycardia, sinus arrest, and conduction disturbances. Severe hypotension may follow intravenous use, particularly (though not exclusively) at rapid infusion rates. Amiodarone may also produce ventricular tachyarrhythmias; torsade de pointes have been reported but appear to be less of a problem with amiodarone than other antiarrhythmics. Rarely, heart failure may be precipitated or aggravated.
Amiodarone reduces the peripheral transformation of thyroxine (T4) to tri-iodothyronine (T3) and increases the formation of reverse-T3
It can affect thyroid function and may induce hypo- or hyperthyroidism.
There have been reports of severe pulmonary toxicity including pulmonary fibrosis and interstitial pneumonitis; these effects are usually reversible on withdrawal of amiodarone but are potentially fatal. pulmonary haemorrhage has also been noted rarely. Amiodarone can adversely affect the liver. There may be abnormal liver function tests and cirrhosis or hepatitis; fatalities have been reported. Prolonged use of amiodarone causes the development of benign yellowish-brown corneal microdeposits in the majority of patients, sometimes associated with coloured haloes of light; these are reversible on stopping therapy. Photosensitivity reactions are also common and more rarely blue -grey discoloration of the skin may occur. Other adverse effects reported include benign intracranial hypertension, haemolytic or aplastic anaemia, peripheral neuropathy, paraesthesias, myopathy, ataxia, tremor, nausea, vomiting, a metallic taste, nightmares, headaches, sleeplessness, fatigue, and epididymitis. Thrombophlebitis can occur if amiodarone is injected regularly or infused for prolonged periods into a peripheral vein. Rapid intravenous injection has been associated with anaphylactic shock, hot flushes, sweating, and nausea.
It has been suggested that amiodarone – induced phospholipidosis may explain some of its adverse effects. Amiodarone's iodine content contributes to its thyrotoxicity.

INTERACTIONS

Amiodarone should be used with caution with other drugs liable to induce bradycardia, such as beta blockers or calcium-channel blockers, and with other antiarrhythmic drugs. Use with arrhythmogenic drugs, particularly drugs that prolong the QT interval such as fluoroquinolones, phenothiazine antipsychotics, tricyclic antidepressants, halofantrine, and terfenadine, should be avoided. Drugs that cause hypokalaernia or hypomagnesaemia may also increase the risk of arrhythmias with amiodarone. Amiodaroneis metabolised by the cytochrome P450 isoenzymesCYP3A4 and CYP2C 8 and interactions may occur with inhibitors of these enzymes, particularly with inhibitors of CYP3A4 such as HIV-protease inhibitors, cimetidine, and grapefruit juice. Enzyme inducers such as rifampicin and phenytoin may reduce amiodarone concentrations. In addition, amiodarone is an inhibitor of some cytochrome P450 isoenzymes, including CYP3A4 and CYP2D6, resulting in higher plasma concentrations of other drugs metabolised by these enzymes. Examples of these include cidosporin, clonazepam. digoxin, flecainide, phenytoin, procainamide, quinidine, simvastatin, and warfarin. Amiodarone also inhibits P-glycoprotein and could affect drugs that are P-glycoprote insubstrates.

INCOMPATIBLE

Amiodarone is incompatible with NaCl 0.9%.
Avoid equipment containing the plasticiser diethylhexyl phthalate (DEHP). Aminophylline, bivalirudin, ceftazidime, digoxin, drotrecoginalfa (activated), furosemide, heparin sodium, imipenem with cilastatin, magnesium sulfate, micafungin, pantoprazole, piperacillin with tazobactam, sodium bicarbonate.

OVERDOSAGE:

Besides supportive measures, prolonged surveillance of the patient is required because of the long biological half of amiodarone. Severe pulse; if necessary beta-agonists or glucagon may be given.

LACTATION

Amiodarone is excreted in breast milk in significant quantities and is therefore contraindicated in breast-feeding mothers.

OVERDOSE SIGNS AND SYMPTOMS

There is no information available regarding overdosage with intravenous amiodarone. Not much information is available regarding acute overdose with oral amiodarone. A few cases of sinus bradycardia, heart block, ventricular tachycardia, torsade de pointes, circulatory failure and hepatic injury have been reported.

Storage: -Store Protected from Light at a temperature not exceeding 30° C.
Improper Storage may be Deteriorate the product
Medicine: - Keep out of reach of children.
Presentation:– 5 Ampoule of 3 ml in a carton.

Manufactured by:
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Care & Cure with Research
American Remedies Healthcare Pvt. Ltd.
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℞ Amiodarone Sterile Concentrate IP

AMERICAN
Amioron 150

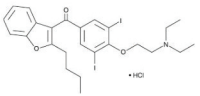
For Intravenous Infusion use only.

Composition:-

Each 3 ml Contains:-
Amiodarone Hydrochloride IP150 mg
Water for Injection IP q.s

DESCRIPTION:-

Amiodarone Sterile Concentrate IP is an antiarrhythmic agent indicated for initiation of treatment and prophylaxis of frequently recurring ventricular fibrillation (VF) and hemodynamically unstable ventricular tachycardia (VT) in patient's refractory to other therapy. Amiodarone Sterile Concentrate IP contains amiodaroneHCl ($C_{25}H_{29}I_2NO_3$ .HCl), a class III antiarrhythmic drug. AmiodaroneHCl is (2-butyl-3-benzo-furanyl)[4-[2-(diethylamino)ethoxy]-3,5diiodophenyl]methanone hydrochloride.AmiodaroneHCl has the following structural formula:



Amiodarone Hydrochloride

PHARMACOLOGY

Amiodarone is absorbed variably and erratically from the gastrointestinal tract; the average bioavailability is about 50%, but varies widely, and both the rate and extent of absorption are Increased by food. It is extensively distributed to body tissues and accumulates notably In fat as well as in skeletal muscles and highly perfused tissues such as liver, lungs, and spleen; it has been reported to be about 96 % bound to plasma proteins. The terminal elimination half-life is about 50 days with a range of about 20 to 100 days due to its extensive tissue distribution. On stopping prolonged amiodarone therapy a pharmacological effect is evident for a month or more. A major metabolite, desethyl-amiodarone, has antiarrhythmic properties. There is very little urinary excretion of amiodarone or its metabolites, the major route of excretion being in faeces via the bile; some enterohepaticrecycling may occur. Amiodarone and desethyl-amiodaroneare reported to cross the placenta and to be distributed into breast milk.
After intravenous injection the maximum effect occurs within 1 to 30 minutes and persists for 1 to 3 hours.

DOSAGE AND ADMINISTRATION

Amiodarone is an antiarrhythmic with mainly class IIIproperties. It is used in the control of ventricular and supraventricular arrhythmias, including arrhythmias associated with Wolff-Parkinson-Whitesyndrome. It has been tried for the prevention of arrhythmias in patients with myocardial infarction or heart failure.
Amiodarone hydrochloride is given orally in initial doses of 200 mg three times daily for a week, then 200 mg twice daily for a week, and then a usual maintenance dosage of 200 mg or less daily, according to response. In the USA, amiodarone is only licensed for ventricular arrhythmias and higher doses are used: loading doses of amiodarone hydrochloride are up to 1.6 g daily for 1 to 3 weeks, followed by 600 to 800 mg daily for a month, then a usual maintenance dose of 400 mg daily. Consideration should be given to potential adverse effects, and patients should be given the minimum effective dose.
Amiodarone hydrochloride may be given intravenously where facilities for close monitoring of cardiac function and resuscitation are available. It is usually given as a dilute solution in glucose 5 %. Solutions containing less than 600 micrograms/mL are unstable but high concentrations are irritating to the veins, and solutions containing more than 2 mg/mL should be given via a central catheter; a central catheter is also preferred if repeated or continuous infusion is required. The usual dose is 1 to 1.2 g over 24 hours, given by intermittent or continuous infusion as follows:

- in the UK, an initial infusion of 5 mg/kg in 250 mL ofglucose 5% is given over 20 to 120 minutes; the infusion may be repeated if required, up to a total dose of 1.2 g in24 hours, diluted in up to 500 mL of glucose 5 %
- in the USA, a n initial dose of 150 mg in 100 mL of glucose5% is given over 10 minutes, followed by 900 mg in500 mL of glucose 5% over 24 hours, given at a rate of1 mg/minute for 6 hours and then 500 micrograms/minute for 18 hours; if necessary the maintenance infusion may be continued at a rate of 500 micrograms/minuteusing a 1 to 6 mg/mL solution
- In emergencies, amiodarone hydrochloride may be givenin doses of 50 to 300 mg in 10 to 20 mL of glucose 5% by slow intravenous injection over a period of not less than3 minutes; a second injection should not be given until atleast 15 minutes after the first For the use of amiodarone in children, see below.

ADMINISTRATION.

Addition of amiodarone hydrochloride to an intravenous infusion solution reduces the drop size delivered and the reduction in size is greater as the concentration of amiodarone is increased. This resulted in a reduction of about 30% in the expected delivery rate when amiodarone hydrochloride 1.2 g was given in 500 mL of glucose 5 %. The reduction in drop size has been attributed to a reduction in surface tension caused by inclusion of Tween 80 (polysorbate 80) in the standard intravenous formulation. Allowances should be made for the changes in drop size causing a reduction of the delivery rate of infusions of amiodarone hydrochloride. US licensed product information for the standard formulation contra-indicates the use of drop-counter infusion sets and requires the use of a volumetric infusion pump when intravenous amiodarone is given.
Aqueous formulations ofamiodarone that do not contain polysorbate 80 have been developed and may be available in some countries,

PRECAUTIONS

Amiodarone should not be given to patients with bradycardia, sino-atrial block, A V block or other severe conduction disorders (unless the patient has a pacemaker), severe hypotension, or severe respiratory failure. It may be used, but with caution, in patients with heart failure. Electrolyte disorders should be corrected before starting treatment. The use of amiodarone should be avoided in patients with iodine sensitivity, or evidence or history of thyroid disorders. Patients taking amiodarone should avoid exposure to sunlight. Thyroid function should be monitored regularly in order to detect amiodarone-induced hyper- or hypothyroidism. Thyroxine, tri-iodothyronine, and thyrotrophin (thyroidstimulatinghormone; TSH) concentrations should be measured; clinical assessment is important but is unreliable alone. See also Effects on Thyroid Function under Adverse
Effects and Treatment. Tests of liver and pulmonary function should also be carried out regularly in patients on long-term therapy.
Ophthalmological examinations should be performed annually. Although urinary excretion is not a major route for the elimination of amiodarone or its metabolites, there is a possibility of iodine accumulation in renal impairment. Intravenous injections of amiodarone should be given slowly: if prolonged or repeated infusions are envisaged, the use of a central